The imposter syndrome, stupidity, and antedisciplinary and mad science: a career analysis

John Wikswo

Vanderbilt University Institute for Imaging Science Friday Seminar

Vanderbilt University

12 November 2021

Backgrounds by Julia Wikswo

Outline

- Imposter syndrome
- Stupidity in science
- Antedisciplinary science
- How people learn
- Intellectual phase space
- Evolution of an interdisciplinary career
- The complexity of biology
- Accelerating biological discovery
- The future of biology
- Reviewing in an interdisciplinary age
- Lessons learned

The Imposter Syndrome

The Impostor Syndrome

- Wikipedia: **Impostor syndrome** (also known as impostor phenomenon, impostorism, fraud syndrome, or the impostor experience) is a psychological pattern in which an individual doubts their skills, talents,or accomplishments and has a persistent internalized fear of being exposed as a "fraud".
- This talk will explain how I overcame this.

Stupidity in Science

The importance of stupidity in scientific research

Martin A. Schwartz
Department of Microbiology, UVA Health System, University of Virginia, Charlottesville, VA 22908, USA
e-mail: maschwartz@virginia.edu

Accepted 9 April 2008
Journal of Cell Science 121, 1771 Published by The Company of Biologists 2008
doi:10.1242/jcs.033340

I recently saw an old friend for the first time in many years. We had been Ph.D. students at the same time, both studying science, although in different areas. She later dropped out of graduate school, went to Harvard Law School and is now a senior lawyer for a major environmental organization. At some point, the conversation turned to why she had left graduate school. To my utter astonishment, she said it was because it made her feel stupid. After a couple of years of feeling stupid every day, she was ready to do something else.

I had thought of her as one of the brightest people I knew and her subsequent career supports that view. What she said bothered me. I kept thinking about it; sometime the next day, it hit me. Science makes me feel stupid too. It's just that I've gotten used to it. So used to it, in fact, that I actively seek out new opportunities to feel stupid. I wouldn't know what to do without that feeling. I even think it's supposed to be this way. Let me explain.

For almost all of us, one of the reasons that we liked science in high school and college is that we were good at it. That can't be the only reason – fascination with understanding the physical world and an emotional need to discover new things has to enter into it too. But high-school and college science means taking courses, and doing well in courses means getting the right answers on tests. If you know those answers, you do well and get to feel smart.

I'd like to suggest that our Ph.D. programs often do students a disservice in two ways. First, I don't think students are made to understand how hard it is to do research. And how very, very hard it is to do important research. It's a lot harder than taking even very demanding courses. What makes it difficult is that research is immersion in the unknown. We just don't know what we're doing. We can't be sure whether we're asking the right question or doing the right experiment until we get the answer or the result. Admittedly, science is made harder by competition for grants and space in top journals. But apart from all of that, doing significant research is intrinsically hard and changing departmental, institutional or national policies will not succeed in lessening its intrinsic difficulty.

Second, we don't do a good enough job of teaching our students how to be productively stupid – that is, if we don't feel stupid it means we're not really trying. I'm not talking about 'relative stupidity', in which the other students in the class actually read the material, think about it and ace the exam, whereas you don't. I'm also not talking about bright people who might be working in areas that don't match their talents. Science involves confronting our 'absolute stupidity'. That kind of stupidity is an existential fact, inherent in our efforts to push our way into the unknown.

The importance of stupidity in scientific research

Martin A. Schwartz
Department of Microbiology, UVA Health System, University of Virginia, Charlottesville, VA 22908, USA
e-mail: maschwartz@virginia.edu

Accepted 9 April 2008
Journal of Cell Science 121, 1771 Published by The Company of Biologists 2008
doi:10.1242/jcs.033340

I recently saw an old friend for the first time in many years. We had been Ph.D. students at the same time, both studying science, although in different areas. She later dropped out of graduate school, went to Harvard Law School and is now a senior lawyer for a major environmental organization. At some point, the conversation turned to why she had left graduate school. To my utter astonishment, she said it was because it made her feel stupid. After a couple of years of feeling stupid every day, she was ready to do something else.

I had thought of her as one of the brightest people I knew and her subsequent career supports that view. What she said bothered me. I kept thinking about it; sometime the next day, it hit me. Science makes me feel stupid too. It's just that I've gotten used to it. So used to it, in fact, that I actively seek out new opportunities to feel stupid. I wouldn't know what to do without that feeling. I even think it's supposed to be this way. Let me explain.

ıms often do students a
k students are made to
nd how very, very hard
r than taking even very
ult is that research is
now what we're doing.
right question or doing
answer or the result.
npetition for grants and
f that, doing significant
partmental, institutional
lessening its intrinsic

of teaching our students
we don't feel stupid it
talking about 'relative
the class actually read
ım, whereas you don't.
who might be working
ce involves confronting
pidity is an existential
vay into the unknown.

The importance of stupidity in scientific research

Martin A. Schwartz
Department of Microbiology, UVA Health System, University of Virginia, Charlottesville, VA 22908, USA
e-mail: maschwartz@virginia.edu

Accepted 9 April 2008
Journal of Cell Science 121, 1771 Published by The Company of Biologists 2008
doi:10.1242/jcs.033340

I recently s
had been P
although in
went to Ha
environme
to why she
said it was
of feeling s
I had th
her subseq
me. I kept t
makes me
used to it, i
stupid. I w
think it's s
For alm
high schoo
the only rea
and an em
too. But hig
doing well
you know t

Productive stupidity means being ignorant by choice. Focusing on important questions puts us in the awkward position of being ignorant. One of the beautiful things about science is that it allows us to bumble along, getting it wrong time after time, and feel perfectly fine as long as we learn something each time. No doubt, this can be difficult for students who are accustomed to getting the answers right. No doubt, reasonable levels of confidence and emotional resilience help, but I think scientific education might do more to ease what is a very big transition: from learning what other people once discovered to making your own discoveries. The more comfortable we become with being stupid, the deeper we will wade into the unknown and the more likely we are to make big discoveries.

Be wary of people who hide their own insecurities by trying to make other people look stupid!

rnal of Cell Science

Antedisciplinary Science

OPEN ACCESS Freely available online PLoS COMPUTATIONAL BIOLOGY

Perspectives

"Antedisciplinary" Science

Sean R. Eddy

"The scale and complexity of today's biomedical research problems demand that scientists move beyond the confines of their individual disciplines and explore new organizational models for team science. Advances in molecular imaging, for example, require collaborations among diverse groups—radiologists, cell biologists, physicists, and computer programmers." —National Institutes of Health Roadmap Initiative [1]

Reading this made me a little depressed. For starters, the phrase "organizational models for team science" makes me imagine a factory floor of scientists toiling away on their next 100-author paper under the watchful gaze of their National Institutes of Health program officers, like some scene from Terry Gilliam's movie *Brazil*. It's also depressing to read that the National Institutes of Health thinks that science has become too hard for individual humans to cope with, and that it will take the hive mind of an interdisciplinary "research team of the future" to make progress. But what's most depressing comes from purely selfish reasons: if groundbreaking science really requires assembling teams of people with proper credentials from different disciplines, then I have made some very bad career moves.

that led us to this. The scale of the genome project required "big science" and large teams. The genome project also fueled the explosive growth of the highly successful field of computational biology. Did the ideas of interdisciplinary science and large teams become inappropriately intertwined? Certainly, achieving the goals of the Human Genome Project required engineers, physicists, and computer scientists. It would be silly to argue against large interdisciplinary teams where a mammoth technical goal can be clearly defined. But when I think of new fields in science that have been opened, I don't think of interdisciplinary *teams* combining existing skills to solve a defined problem—I think of single interdisciplinary *people* inventing new ways to look at the world.

Focusing on interdisciplinary teams instead of interdisciplinary people reinforces standard disciplinary boundaries rather than breaking them down. An interdisciplinary team is a committee in which members identify themselves as an expert in something else besides the actual scientific problem at hand, and abdicate responsibility for the majority of the work because it's not their field. Expecting a team of disciplinary scientists to develop a new field is like sending a team of monolingual diplomats to the United Nations.

Progress is driven by new scientific questions, which demand new ways of thinking. You want to go where a

Citation: Eddy SR (2005) "Antedisciplinary" science. PLoS Comp Biol 1(1): e6.

OPEN ACCESS Freely available online

PLoS COMPUTATIONAL BIOLOGY

Perspectives

"Antedisciplinary" Science

Sean R. Eddy

"The scale and complexity of today's biomedical research problems demand that scientists move beyond the confines of their individual disciplines and explore new organizational models for team science.

that led us to this. The scale of the genome project required "big science" and large teams. The genome project also fueled the explosive growth of the highly successful field of computational biology. Did the ideas of interdisciplinary

To encourage the rise of new disciplines as successful as molecular biology, we need to encourage individuals to leave old disciplines behind and forge new fields. New science needs to be judged on its merits, not by the disciplinary credentials of the people doing it—particularly in fast-moving interdisciplinary areas where any formal training may be outdated anyway. If your grant proposal includes statistical analysis, your reviewers shouldn't be acting as enforcers requiring you to have a card-carrying statistician as a collaborator. Maybe in your narrow area, you know how to do the relevant statistics as well as any formally trained statistician. A proposal invoking high-performance comput-

Citation: Eddy SR (2005) "Antedisciplinary" science. PLoS Comp Biol 1(1): e6.

OPEN ACCESS Freely available online

PLoS COMPUTATIONAL BIOLOGY

Perspectives

"Antedisciplinary" Science

Sean R. Eddy

"The scale and complexity of today's biomedical research problems demand that scientists move beyond the confines of their individual disciplines and explore new organizational models for team science. Advances in molecular imaging, for example, require collaborations among diverse groups—radiologists, cell biologists, physicists, and computer programmers." —National Institutes of Health Roadmap Initiative [1]

Reading this made me a little depressed. For starters, the phrase "organizational models for team science" makes me imagine a factory floor of scientists toiling away on their
of their Natio
some scene fr
depressing to
thinks that sc
humans to co
interdisciplin
progress. But
selfish reason
assembling te[...]
different disciplines, then I have made some very bad career moves.

that led us to this. The scale of the genome project required "big science" and large teams. The genome project also fueled the explosive growth of the highly successful field of computational biology. Did the ideas of interdisciplinary science and large teams become inappropriately intertwined? Certainly, achieving the goals of the Human Genome Project required engineers, physicists, and computer scientists. It would be silly to argue against large interdisciplinary teams where a mammoth technical goal can be clearly defined. But when I think of new fields in science that have been opened, I don't think of interdisciplinary *teams* combining existing skills to solve a defined problem—I think of single interdisciplinary

Perhaps the whole idea of interdisciplinary science is the wrong way to look at what we want to encourage. What we really mean is "antedisciplinary" science—the science that precedes the organization of new disciplines, the Wild West frontier stage that comes before the law arrives. It's apropos

team of monolingual diplomats to the United Nations.

Progress is driven by new scientific questions, which demand new ways of thinking. You want to go where a

Citation: Eddy SR (2005) "Antedisciplinary" science. PLoS Comp Biol 1(1): e6.

OPEN ACCESS Freely available online

PLoS COMPUTATIONAL BIOLOGY

Perspectives

"Antedisciplinary" Science

Sean R. Eddy

that led us to this. The scale of the genome project required

"The scale and con
demand that scient
disciplines and exp
Advances in molec
among diverse grou
computer program
Initiative [1]

Reading t
the phra
makes m
away on their ne
of their Nationa
some scene from
depressing to re
thinks that scien
humans to cope
interdisciplinary
progress. But wh
selfish reasons: i
assembling team
different discipli
moves.

One can't deny that science is getting more complex, because the sheer amount of knowledge is growing. But the history of science is full of ideas that seemed radical, unfathomable, and interdisciplinary at the time, but that now we teach to undergraduates. Every generation, we somehow compress our knowledge just enough to leave room in our brains for one more generation of progress. This is not going to stop. It may take big interdisciplinary teams to achieve certain technical goals as they come tantalizingly within view, but someone also needs to synthesize new knowledge and make it useful to individual human minds, so the next generation will have a taller set of giants' shoulders to stand on. Computer science mythologizes the big teams and great

Citation: Eddy SR (2005) "Antedisciplinary" science. PLoS Comp Biol 1(1): e6.

How does a person learn?

Simon Shaw - Pew Charitable Trust

“Lieber Gott, lass Hirn vom Himmel fallen!”

“For the love of God, drop some brain from the sky!”

Simon Shaw - Pew Charitable Trust

The mind is not a vessel to be filled but a fire to be kindled.

Plutarch

Wikswo's Teaching Philosophy

The mind is not a vessel to be filled but a fire to be kindled.

Plutarch

You cannot teach a man anything; you can only help him to find it within himself.

Galileo

Education is what survives when what you have learned is forgotten.

B.F. Skinner

If the fool would persist in his folly he would become wise.

Lao Tzu in Tao Te Ching

Everyone's Roles

- I learned by teaching, not by being lectured to.
- Students must teach themselves.
- My role as a teacher is to
  - Determine what students don't know,
  - Discover why they are confused,
  - Encourage them to help each other toward the answers.
- The student's role is to
  - Ask questions.
  - Don't raise hands,
  - Help their colleagues by asking and answering questions,
  - Learn to think beyond their experience,
  - Provide feedback.

How fast do we learn?

Given your total knowledge K, your learning rate is dK/dt

How fast do we learn?

Given your total knowledge K, your learning rate is dK/dt

$$dK/dt = k_L Q_{IN} W_L \ \ldots$$

where

k_L how good you are at learning,

Q_{IN} knowledge flux to which you are exposed,

W_L how hard you work learning,

How fast do we learn?

Given your total knowledge K, your learning rate is dK/dt

$$dK / dt = k_L Q_{IN} W_L - k_F K W_F \quad \ldots$$

where

k_L how good you are at learning,

Q_{IN} knowledge flux to which you are exposed,

W_L how hard you work learning,

k_F how easily you forget,

W_F how hard you work to forget,

How fast do we learn?

Given your total knowledge K, your learning rate is dK/dt

$$dK / dt = k_L Q_{IN} W_L - k_F K W_F + k_S K W_S \ \ldots$$

where

k_L	how good you are at learning,
Q_{IN}	knowledge flux to which you are exposed,
W_L	how hard you work learning,
k_F	how easily you forget,
W_F	how hard you work to forget,
k_S	how good you are at synthesizing new knowledge from what you already know,
W_S	how hard you work synthesizing new knowledge,

How fast do we learn?

Given your total knowledge K, your learning rate is dK/dt

$$dK/dt = k_L Q_{IN} W_L - k_F K W_F + k_S K W_S + k_M M (W_L + W_S - W_F) \ldots$$

where

k_L	how good you are at learning,
Q_{IN}	knowledge flux to which you are exposed,
W_L	how hard you work learning,
k_F	how easily you forget,
W_F	how hard you work to forget,
k_S	how good you are at synthesizing new knowledge from what you already know,
W_S	how hard you work synthesizing new knowledge,
k_M	how good you are at learning from your mistakes,
M	mistake base to which you are exposed,

How fast do we learn?

Given your total knowledge K, your learning rate is dK/dt

$$dK/dt = k_L Q_{IN} W_L - k_F K W_F + k_S K W_S + k_M M (W_L + W_S - W_F) + k_T K W_T$$

where

k_L	how good you are at learning,
Q_{IN}	knowledge flux to which you are exposed,
W_L	how hard you work learning,
k_F	how easily you forget,
W_F	how hard you work to forget,
k_S	how good you are at synthesizing new knowledge from what you already know,
W_S	how hard you work synthesizing new knowledge,
k_M	how good you are at learning from your mistakes,
M	mistake base to which you are exposed,
k_T	how good you are at learning from teaching,
W_T	how hard you work teaching,

How fast do we make mistakes?

Given your total knowledge K, your learning rate is dK/dt

$$dK/dt = k_L Q_{IN} W_L - k_F K W_F + k_S K W_S + k_M M (W_L + W_S - W_F) + k_T K W_T$$

where

k_L how good you are at learning,

Q_{IN} knowledge flux to which you are exposed,

W_L how hard you work learning,

k_F how easily you forget,

W_F how hard you work to forget,

k_S how good you are at synthesizing new knowledge from what you already know,

W_S how hard you work synthesizing new knowledge,

k_M how good you are at learning from your mistakes,

M mistake base to which you are exposed,

k_T how good you are at learning from teaching,

W_T how hard you work teaching,

$$dM/dt = (k_E K - k_M M)(W_L + W_F + W_S + W_T)$$

where

dM/dt the rate at which you make mistakes

k_E your error rate

What are the limits to what a single person can learn?

- Learning rate

$$dK/dt = k_L Q_{IN} W_L - k_F K W_F + k_S K W_S + k_M M(W_L + W_S - W_F) + k_T K W_T$$

- Maximum brain capacity K_{max}
- Rate of knowledge evaporation $k_F K W_F$
- Skill at compressing data to increase $K_{max}^{effective}$
  - Simplifications
  - Connections
- There are many problems that one person cannot solve in a lifetime.

What are the limits to what a <u>community</u> of people can learn?

- For one person, we had

$$dK/dt = k_L Q_{IN} W_L - k_F K W_F + k_S K W_S + k_M M(W_L + W_S - W_F) + k_T K W_T$$

- Let's just add N people, each of whose brain has capacity K_{max} …
- With collective intelligence, the learning rate may scale as $dK/dt\ N^{\gamma}$, $\gamma > 1$
- Maximum brain capacity NK_{max} scales with N
- Distributed memory may reduce knowledge evaporation rate $k_F K W_F$
- Improved learning from mistakes due to redundant error checking
- With experience, utilize knowledge compression to increase $K_{max}^{effective}$
  - Simplifications
  - Connections
- There will still be problems we can't solve fast enough. We will return to this…

The Conundrum

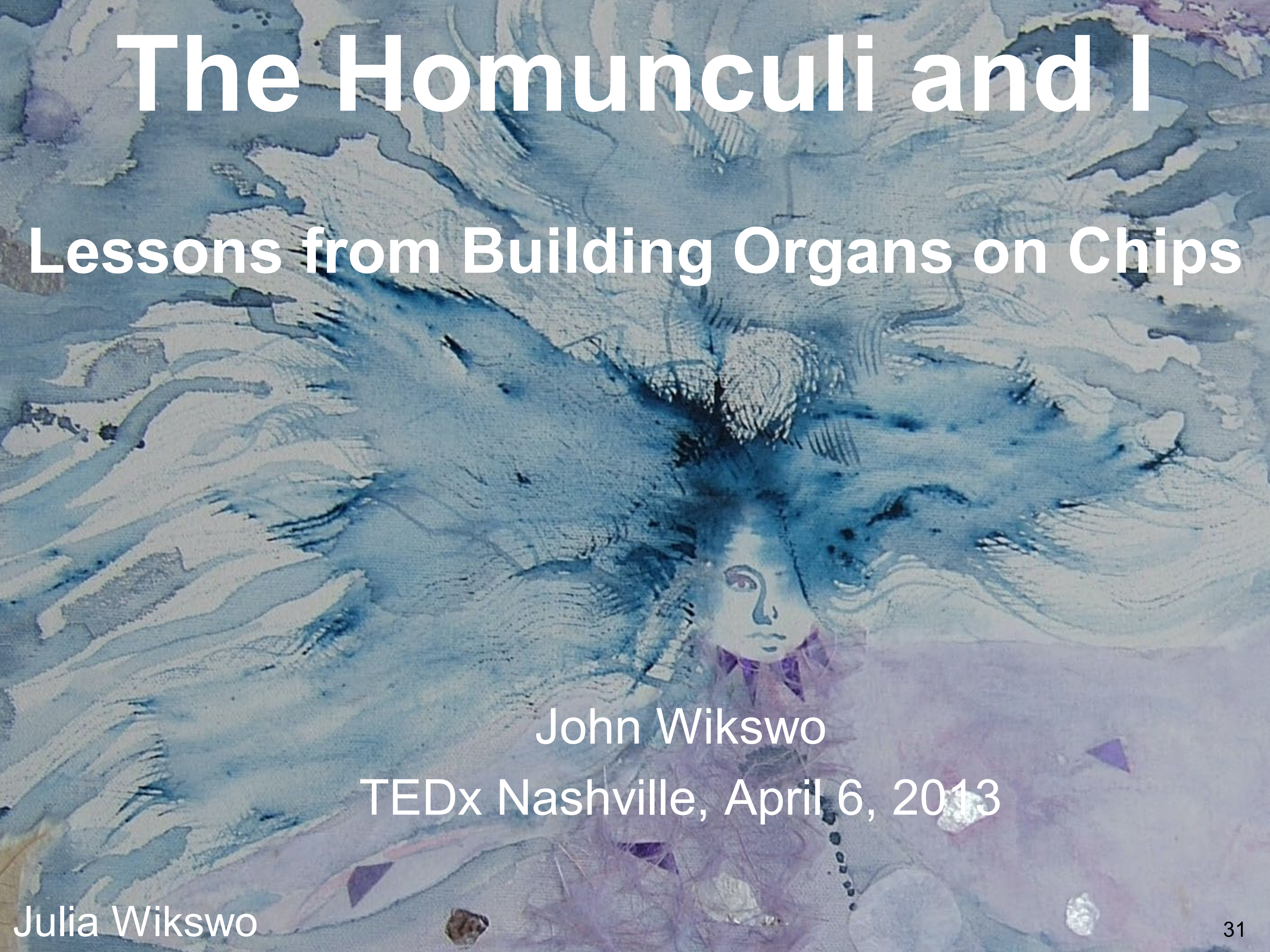
- If you don’t forget or can’t compress your knowledge, you may run out of learning room.
- You don’t always learn by being taught.
- You learn by teaching and by making mistakes.
- If you’re in one of my classes, I learn from you (and my mistakes). *You’re on your own*.
- A successful course is an emergent phenomenon springing from a classroom filled with interacting minds.

How we should learn and teach?

- **Learning tools**: *SPSS, Matlab, Mathematica…*
- **Teach people to *THINK*** rather than *REMEMBER*
- **Teach yourself** from good books/computers
- **Database mining:** Use Google as your memory rather than rote memorization
- **Reward curiosity:** encourage questions without raising hands

Adapted from Simon Shaw - Pew Charitable Trust

Intellectual Phase Space



The Homunculi and I

Lessons from Building Organs on Chips

John Wikswo

TEDx Nashville, April 6, 2013

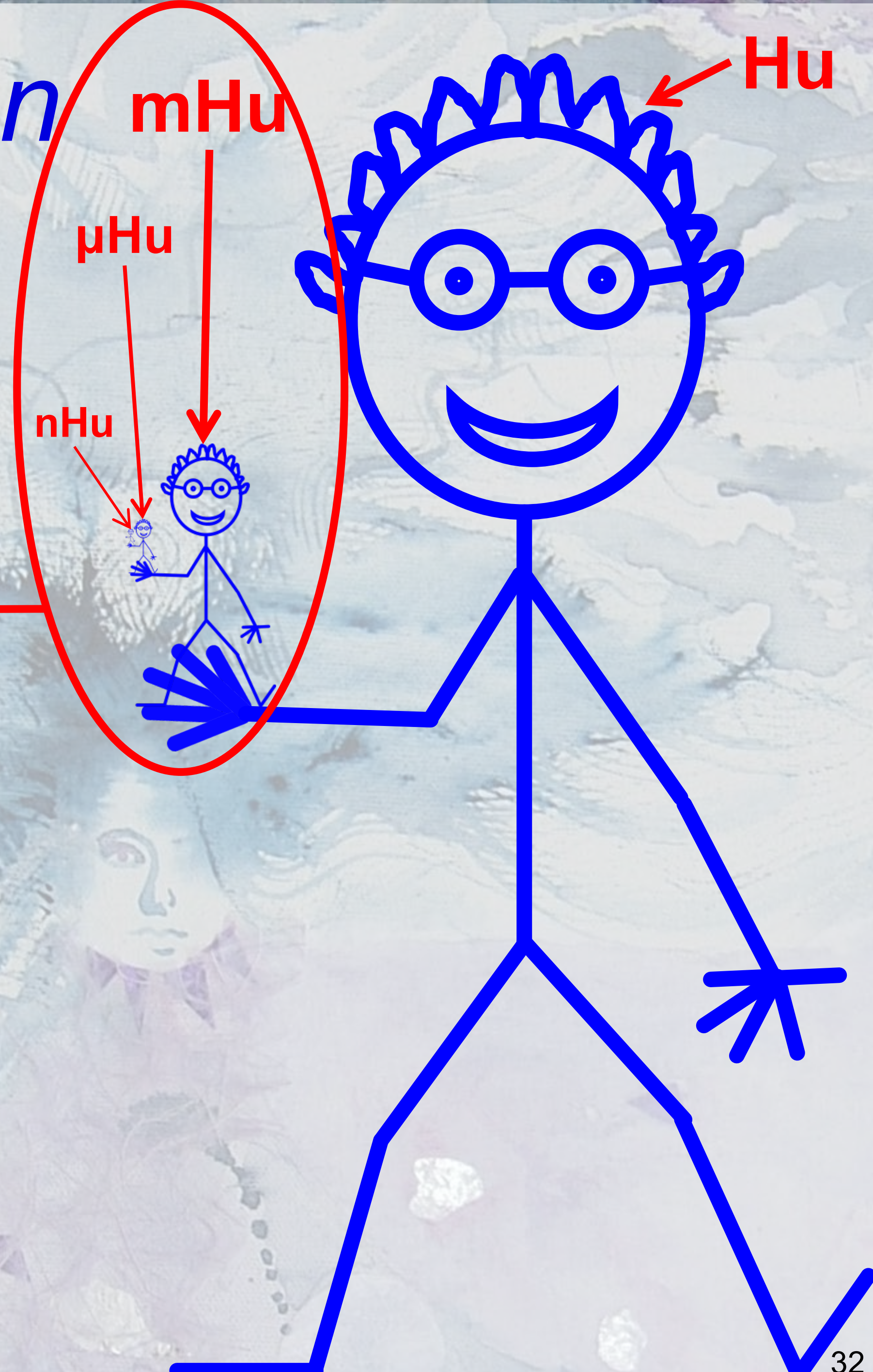
Julia Wikswo

Homunculus, *noun*

[hō-ˈməŋ-kyə-ləs]

plural ho·mun·cu·li

A miniature representation of a human.



Why are we building homunculi?

- Human biology is complex
- Homunculi can simplify:
  - –Drug development
  - –Environmental toxicology
  - –Physiology

Have you or a friend ever had an adverse drug reaction?

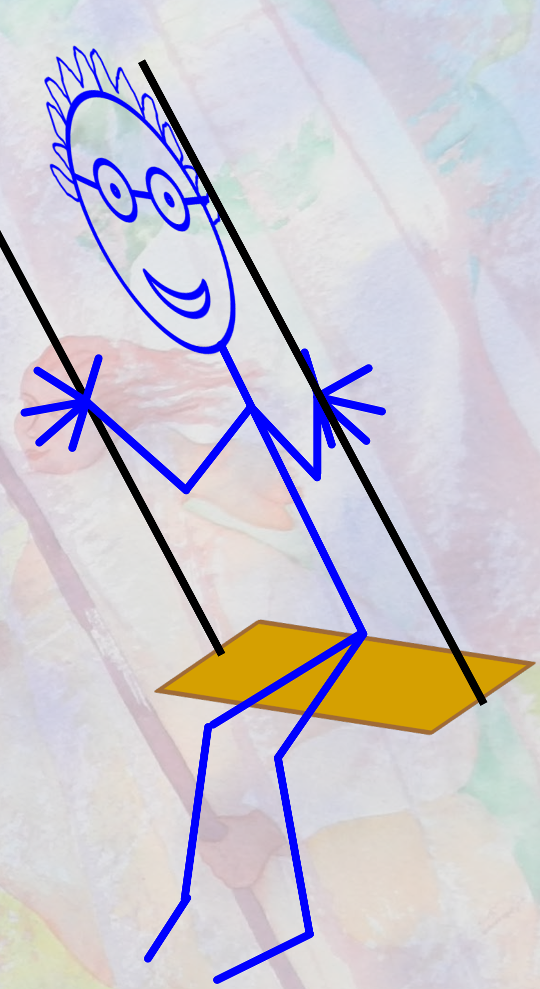
Do household cleaners, garden chemicals, or air pollution bother you?

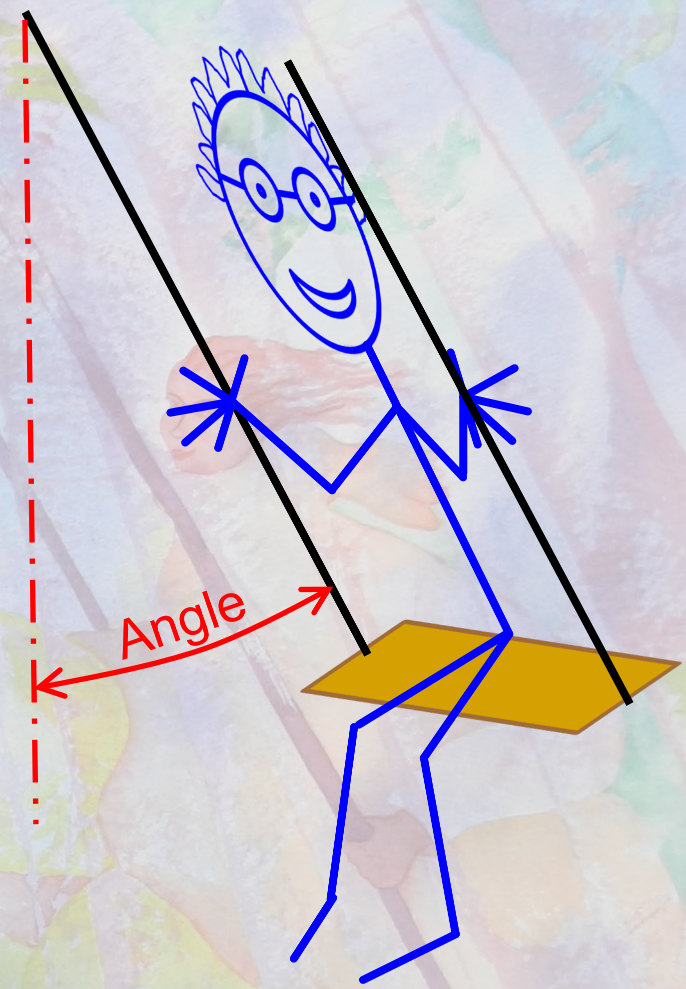
Multidimensional phase space illustrates the variables that affect homonculi and the physicians, scientists and engineers building them.

Phase space

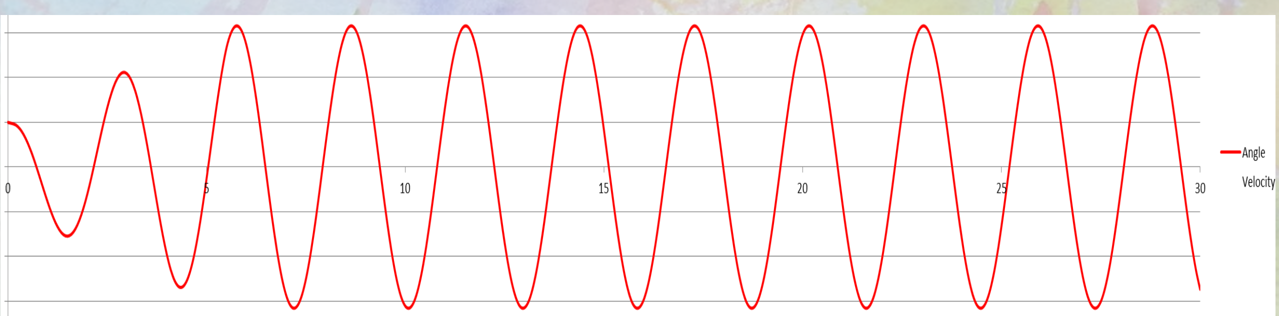
[fāz spās], noun

A geometrical space in which each possible state of a system is represented by a single point.



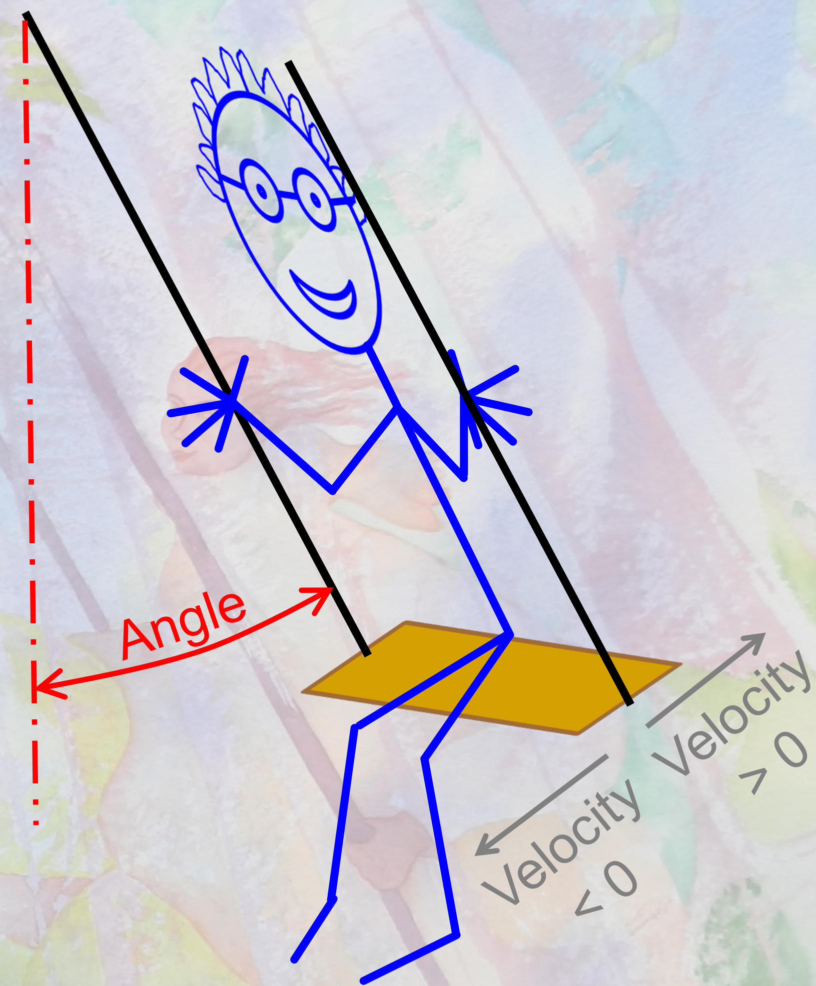


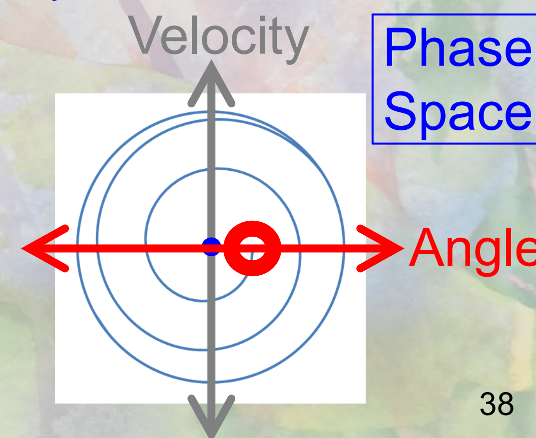
One axis in phase space can represent the range of one variable.



Phase Space

There are as many axes as variables.





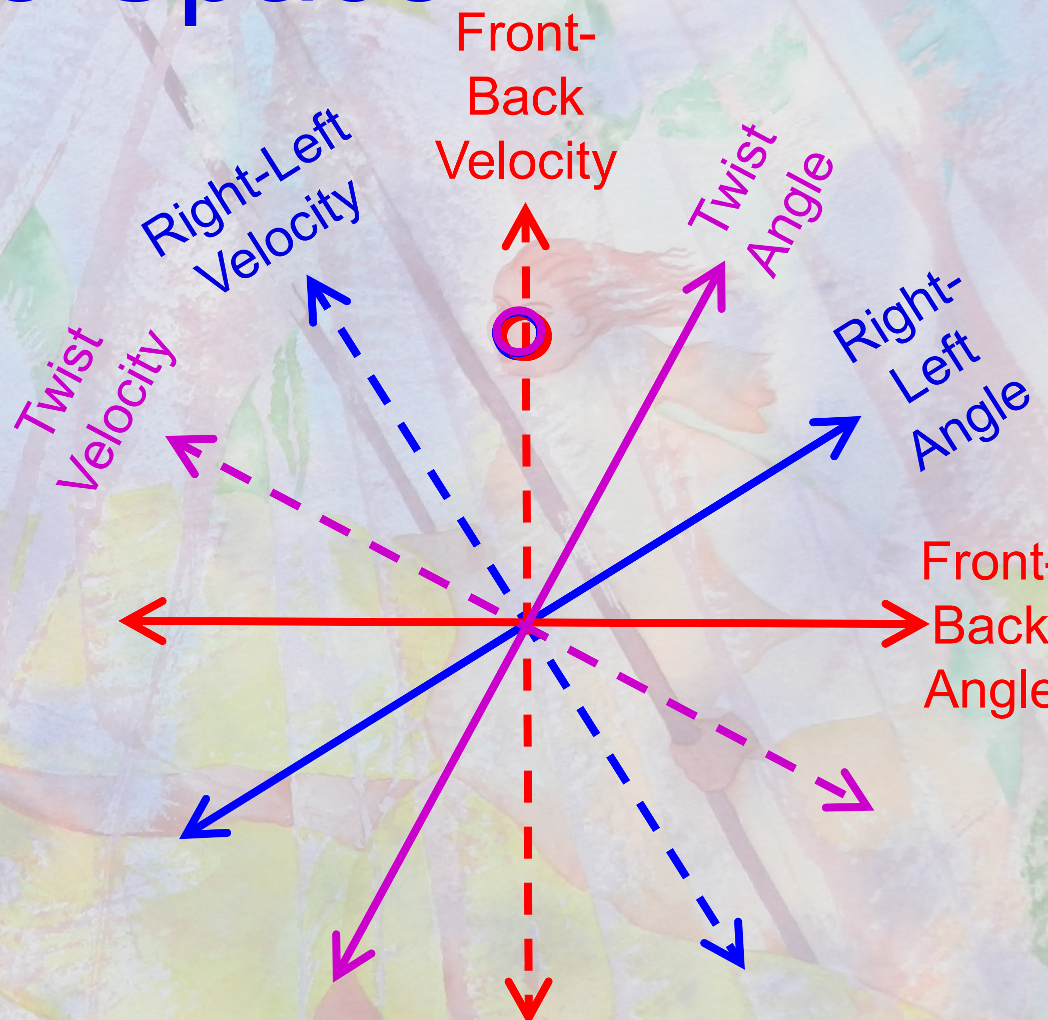
Swing Phase Space

Front and back

Left and Right

Orbit

Twist



Six-Dimensional Phase Space is fun!

You can do lots of things at one time!

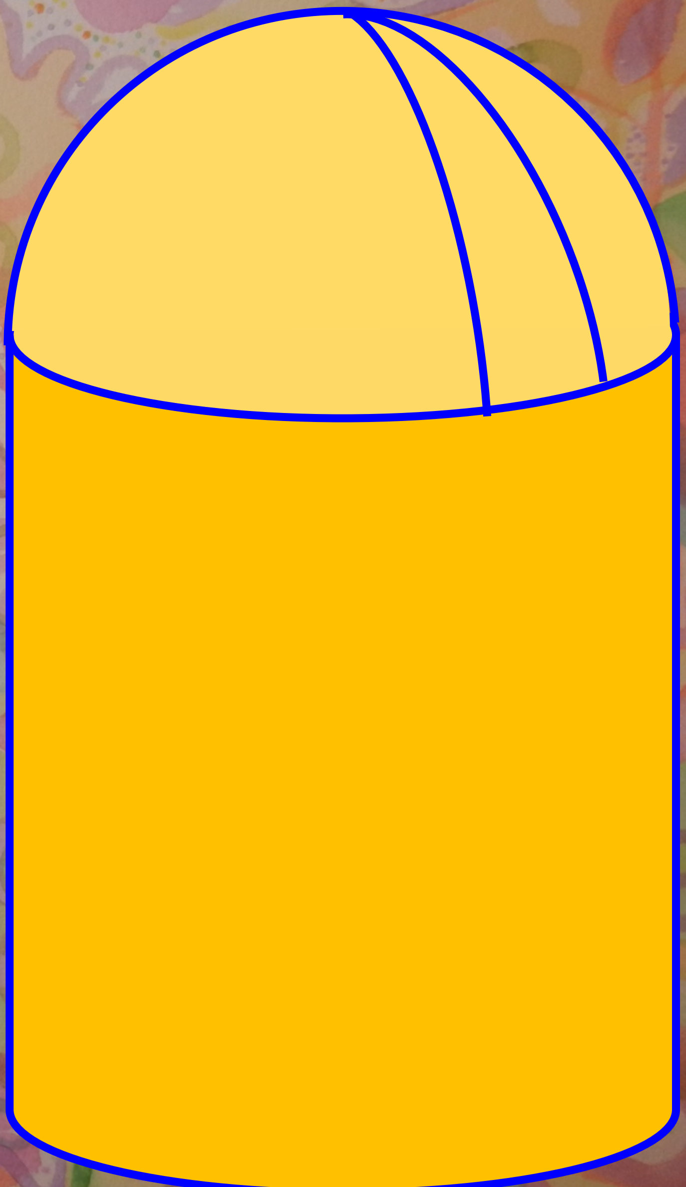
Organs, Organs, Organs

Part of the problem is that human biology is COMPLEX.

- Organs talk to each other, but we seldom hear what they are saying.

Silo -- A place to store stuff without mixing.

Silo Mentality -- Thinking without mixing.



Organ Silos

Thyroid
Pituitary
Adrenals
Brain
Lungs
Kidney
Heart
Liver
Eyes
Skin
Ears
Intestines
Gall Bladder
Pancreas
Spleen
Prostate
Uterus
Ovaries
Testis

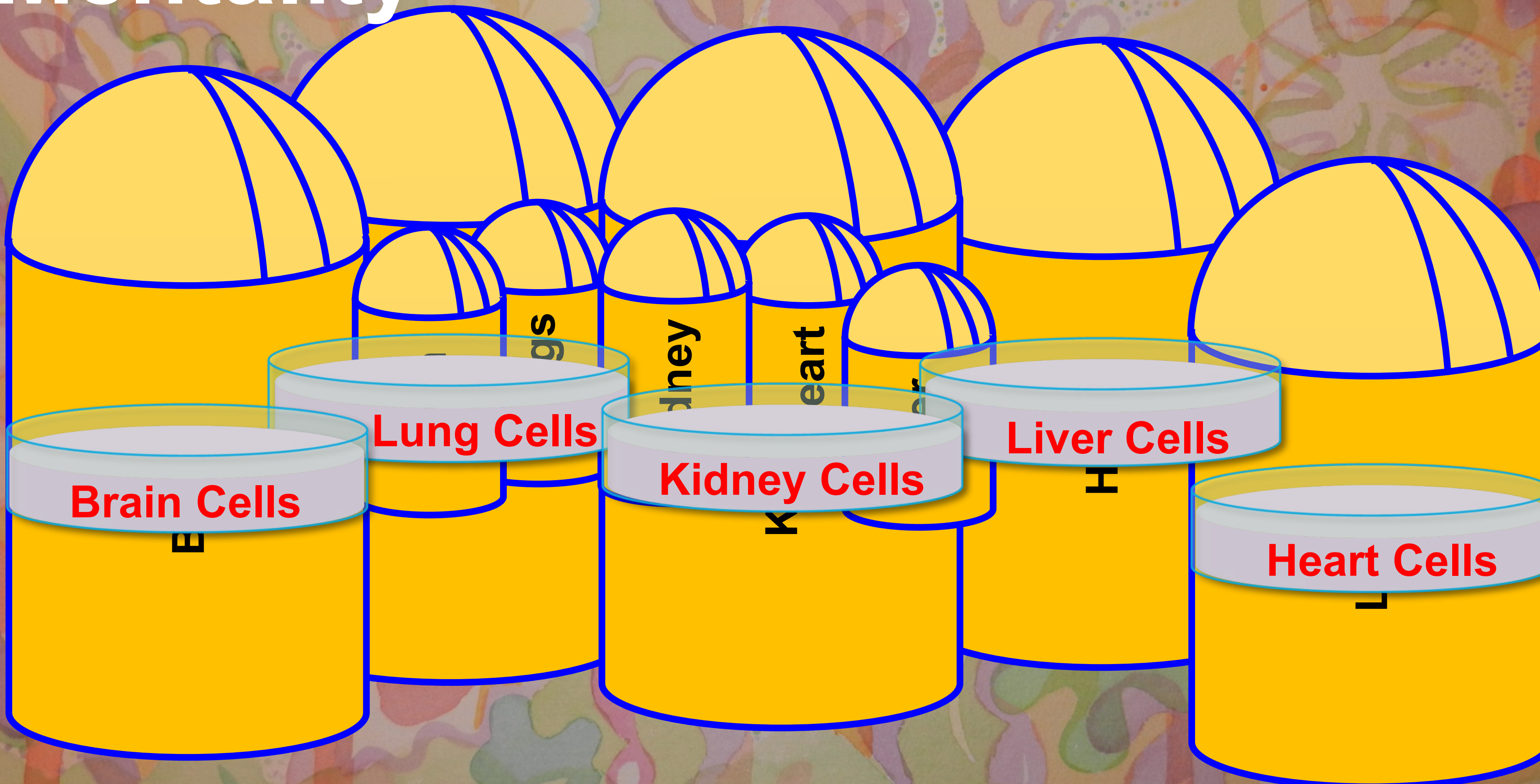
How is a new drug tested?

Petri dishes ⇦

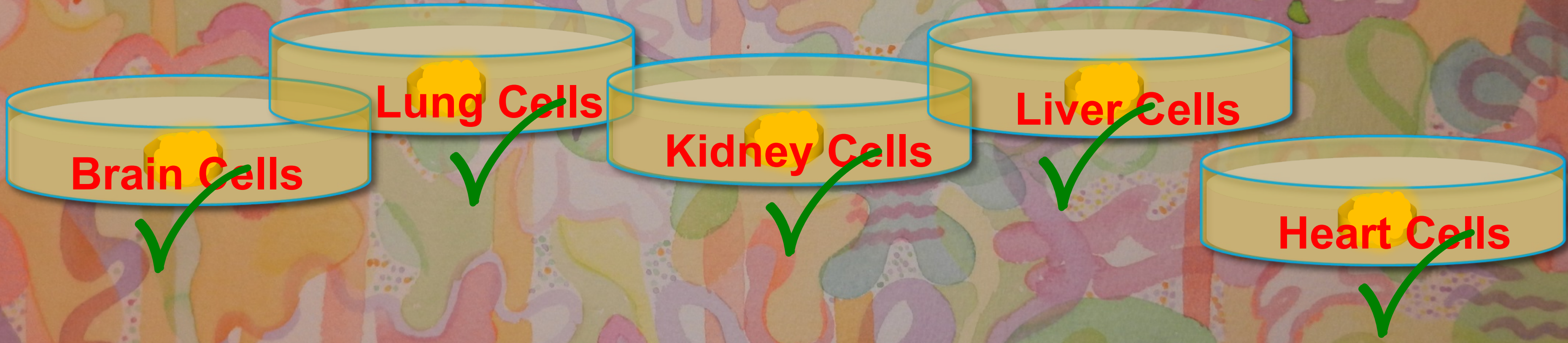
Mice

Humans

Organs from a Silo Mentality
Mentality



Testing drugs in Petri Dishes



How is a new drug tested?

Petri dishes

Mice ⇦

Humans

If each individual "organ" is OK, start testing that drug on mice.

Test drug in mice...

How is a new drug tested?

Petri dishes

Mice

If the mice are OK, then the drug is tested on humans.

Humans

Test drug in humans…

What went wrong?

- **Human genes ≠ mouse genes?**
- **Organ-organ interactions?**

How is a new drug tested?

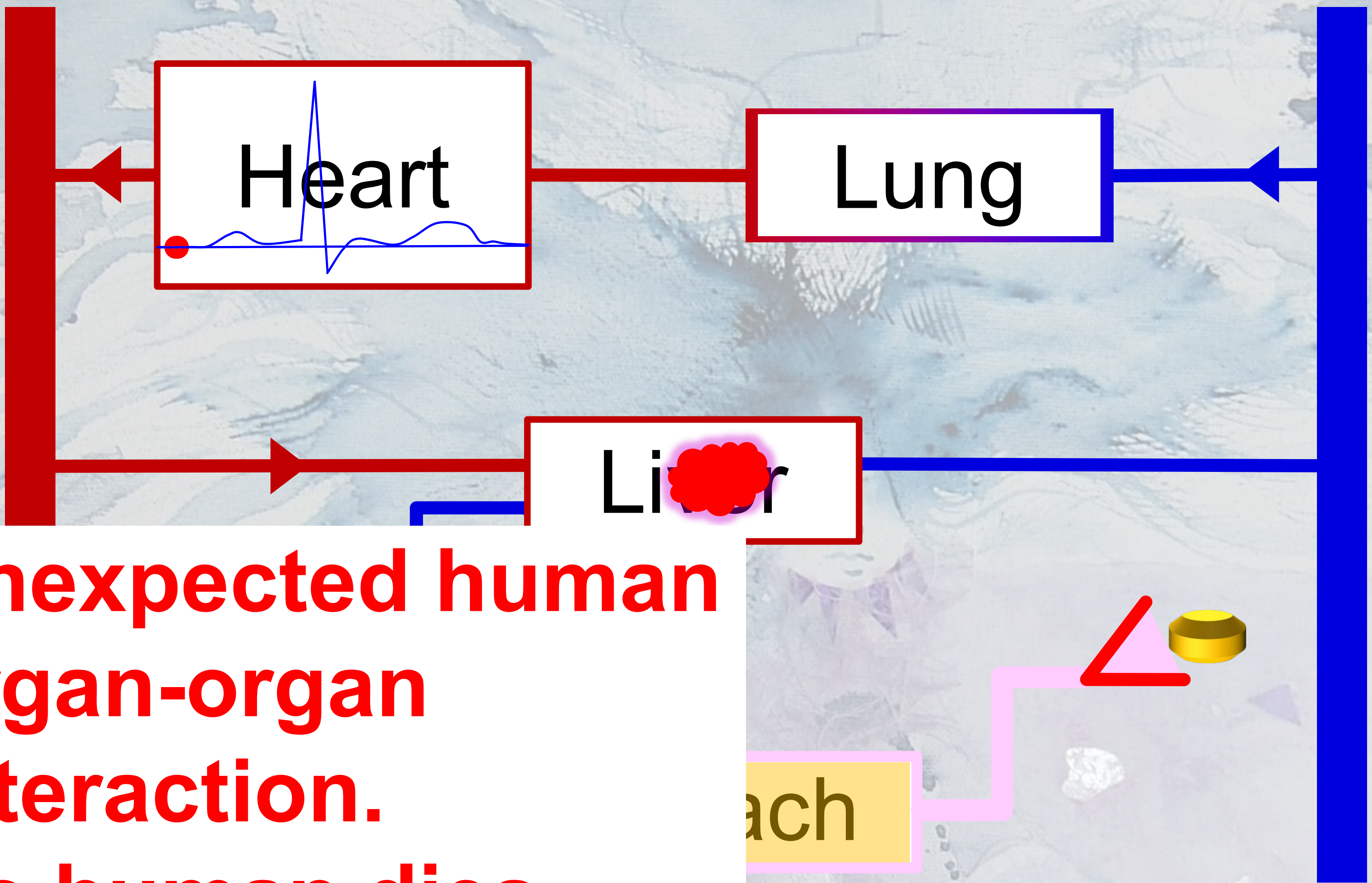
Petri dishes ✓

Mice ✓

Humans ✗

Our homunculi will be alive, built with human cells!

Test drugs in homunculi!



Unexpected human organ-organ interaction.
No human dies.

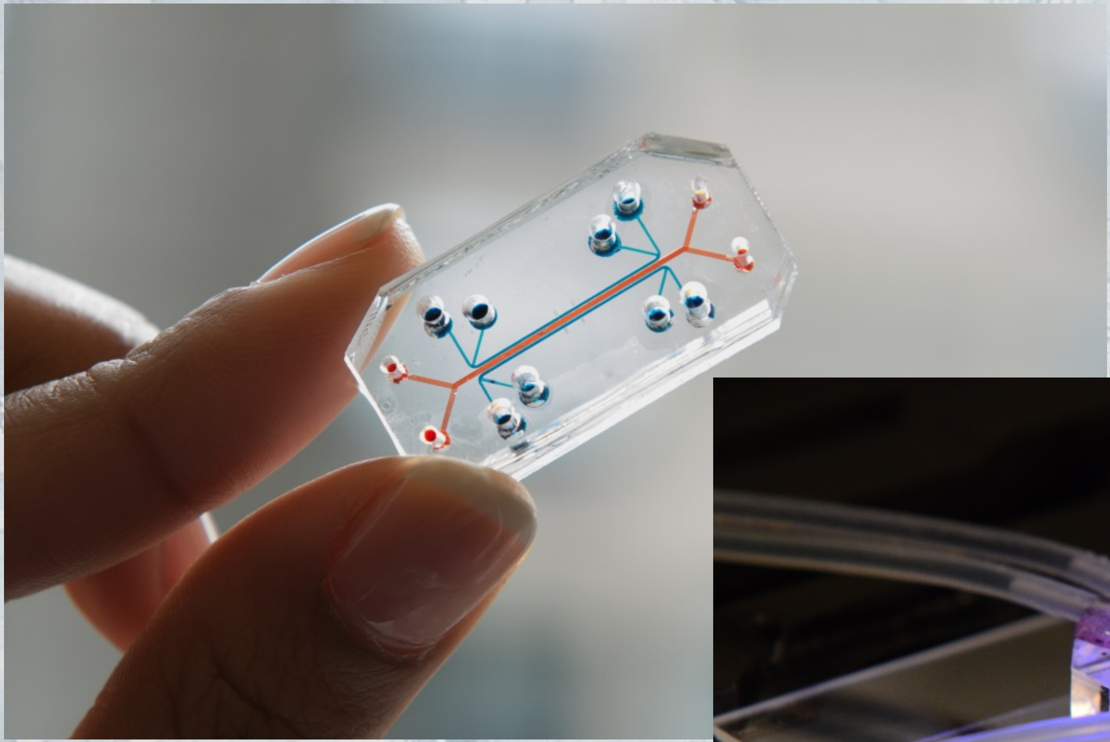
We’ve just seen why we are building homunculi

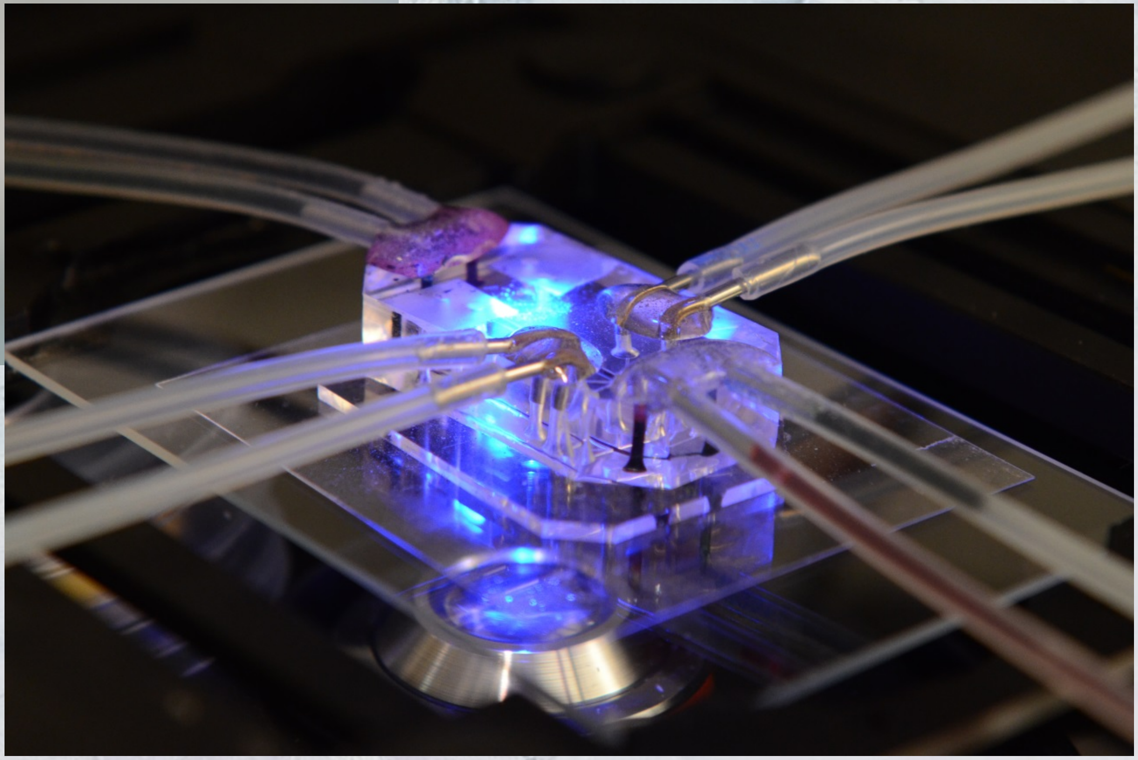
- Human biology is complex
- Homunculi can simplify:
  - Drug development
  - Environmental toxicology
  - Physiology

How do you build homunculi?

- Use human cells to make *microfluidic organ chips* that work like the real organs.
- Connect organs together.
- Do lots of things at the same time. (phase space)

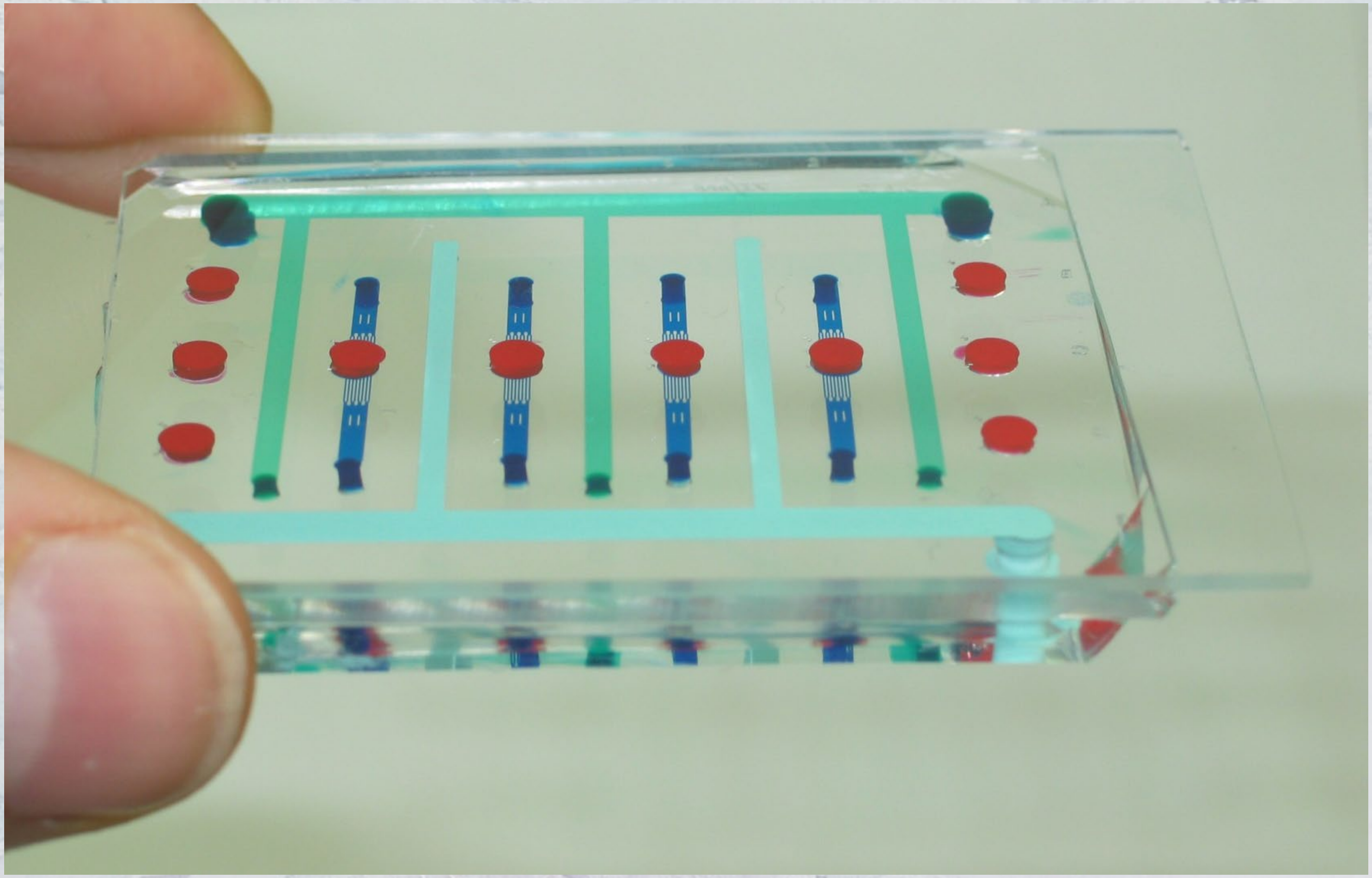
Lung on a chip





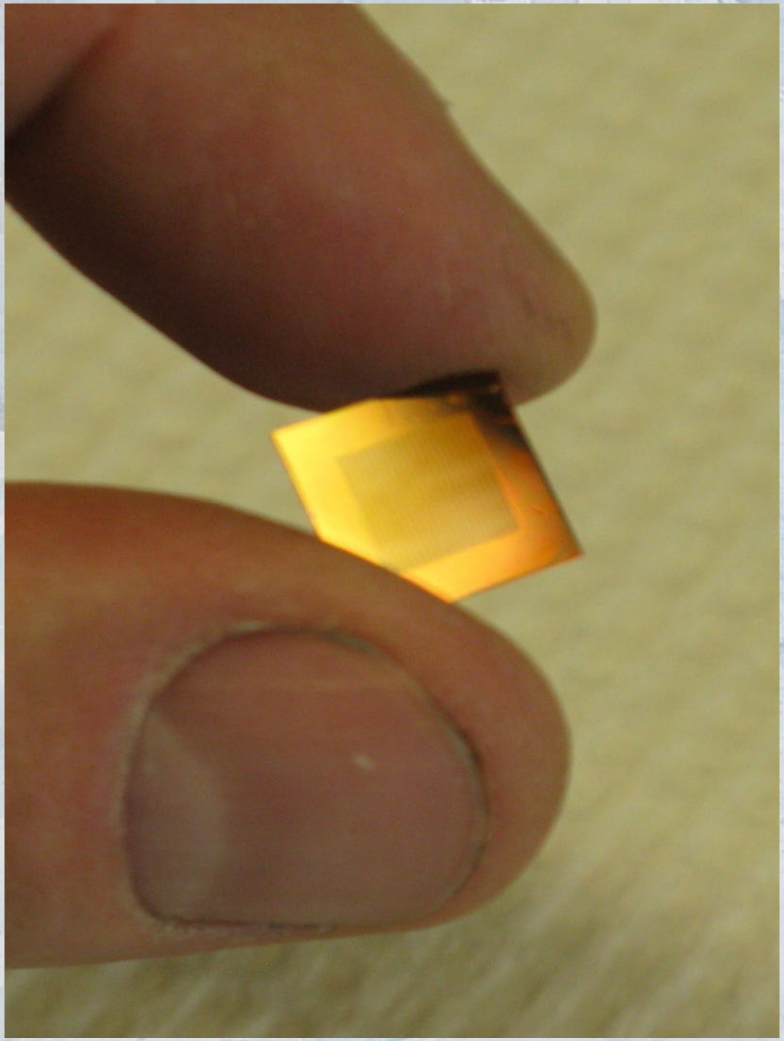
Courtesy of Don Ingber

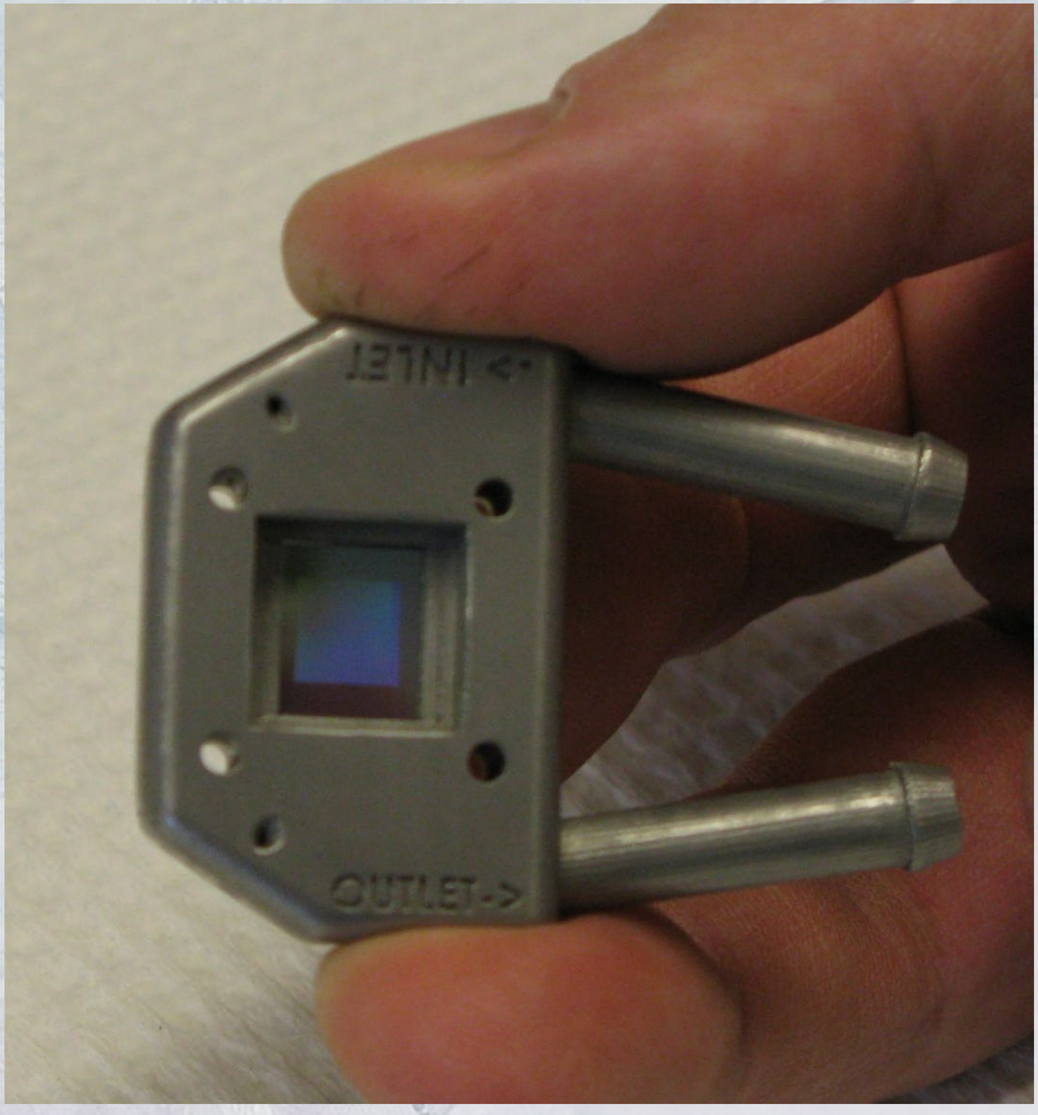
Mammary gland on a chip



Courtesy of Lisa McCawley and Dmitry Markov

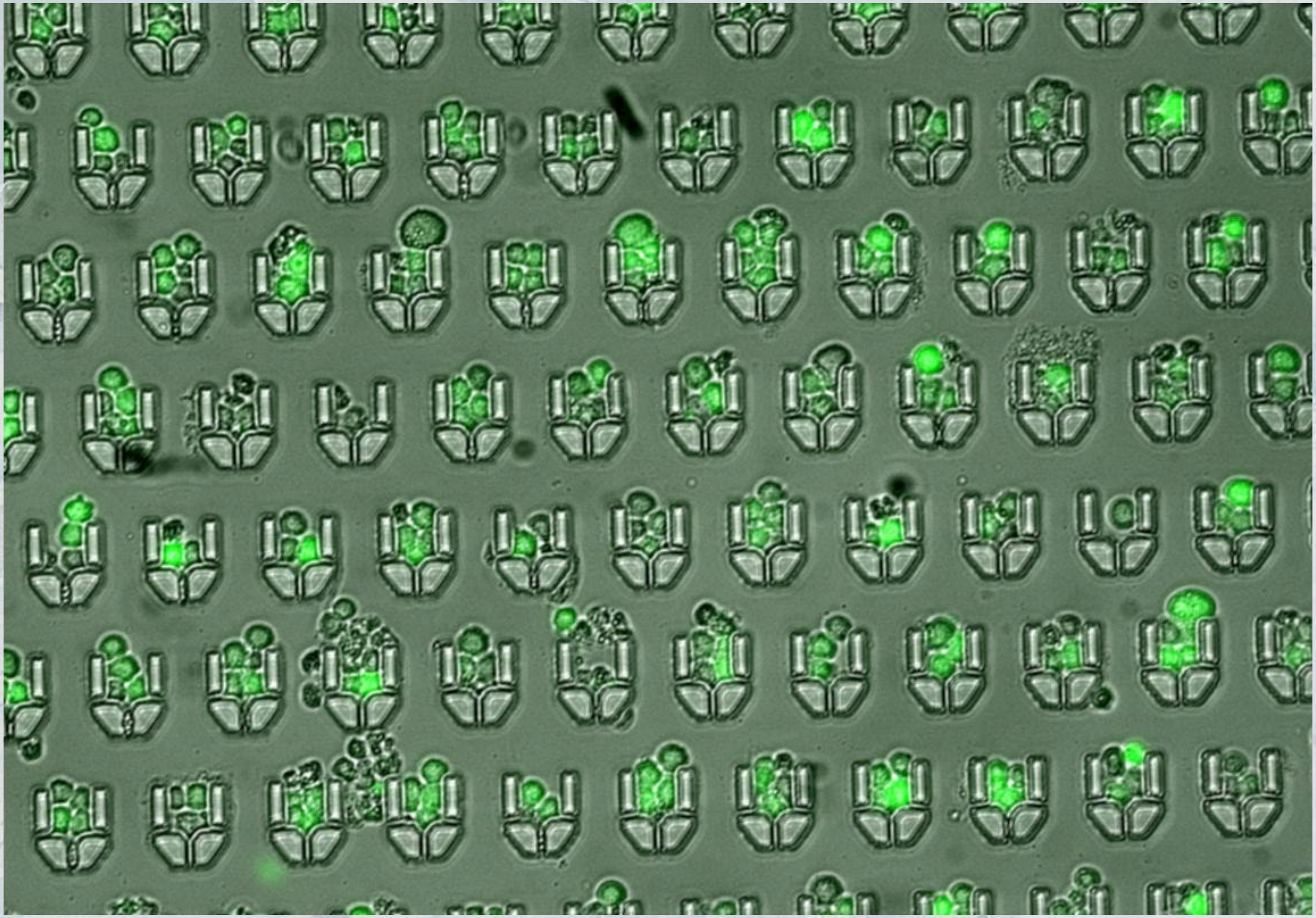
Kidney on a chip





Courtesy of Bill Fissell

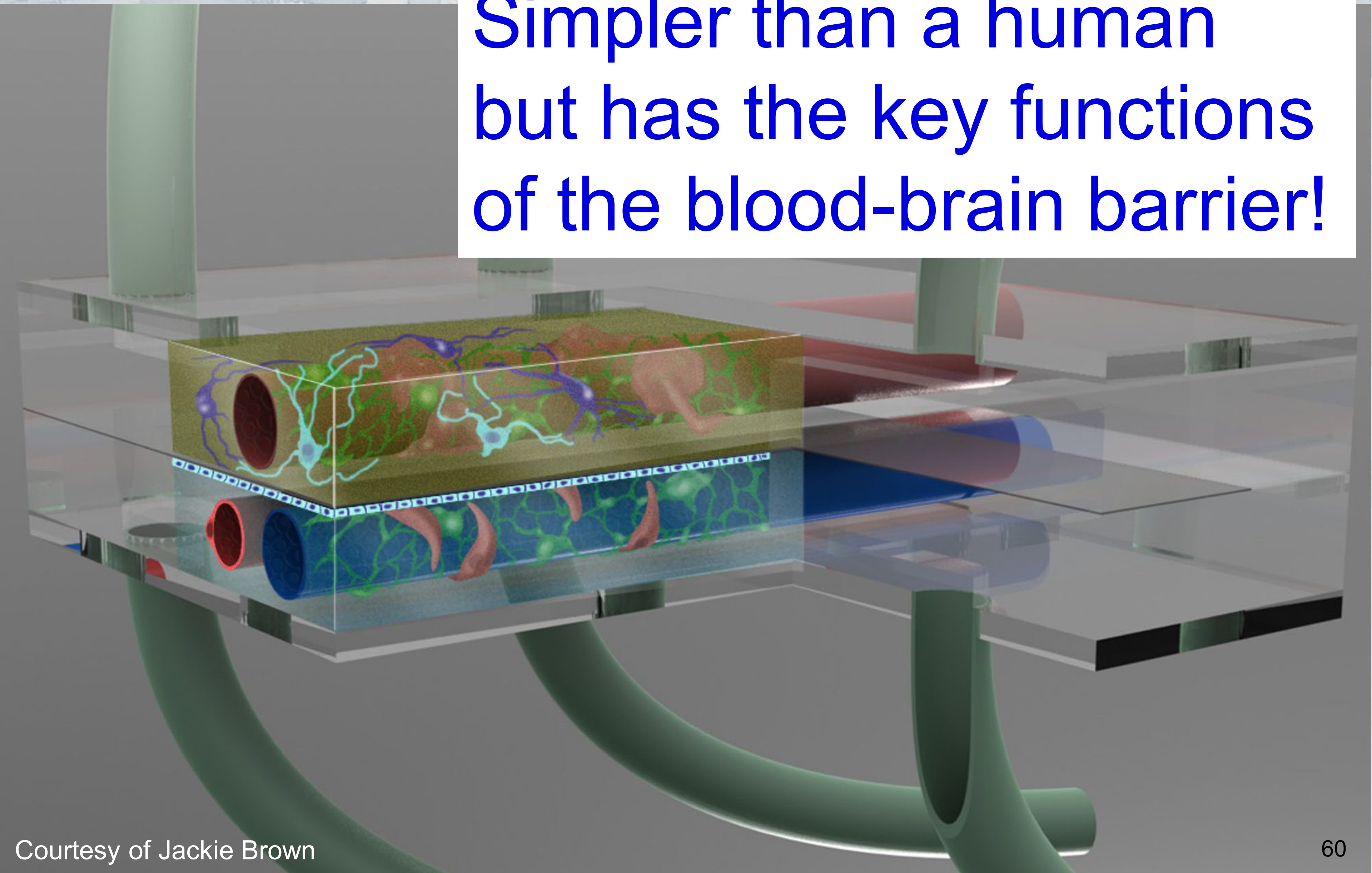
T cells in a lymph node on a chip



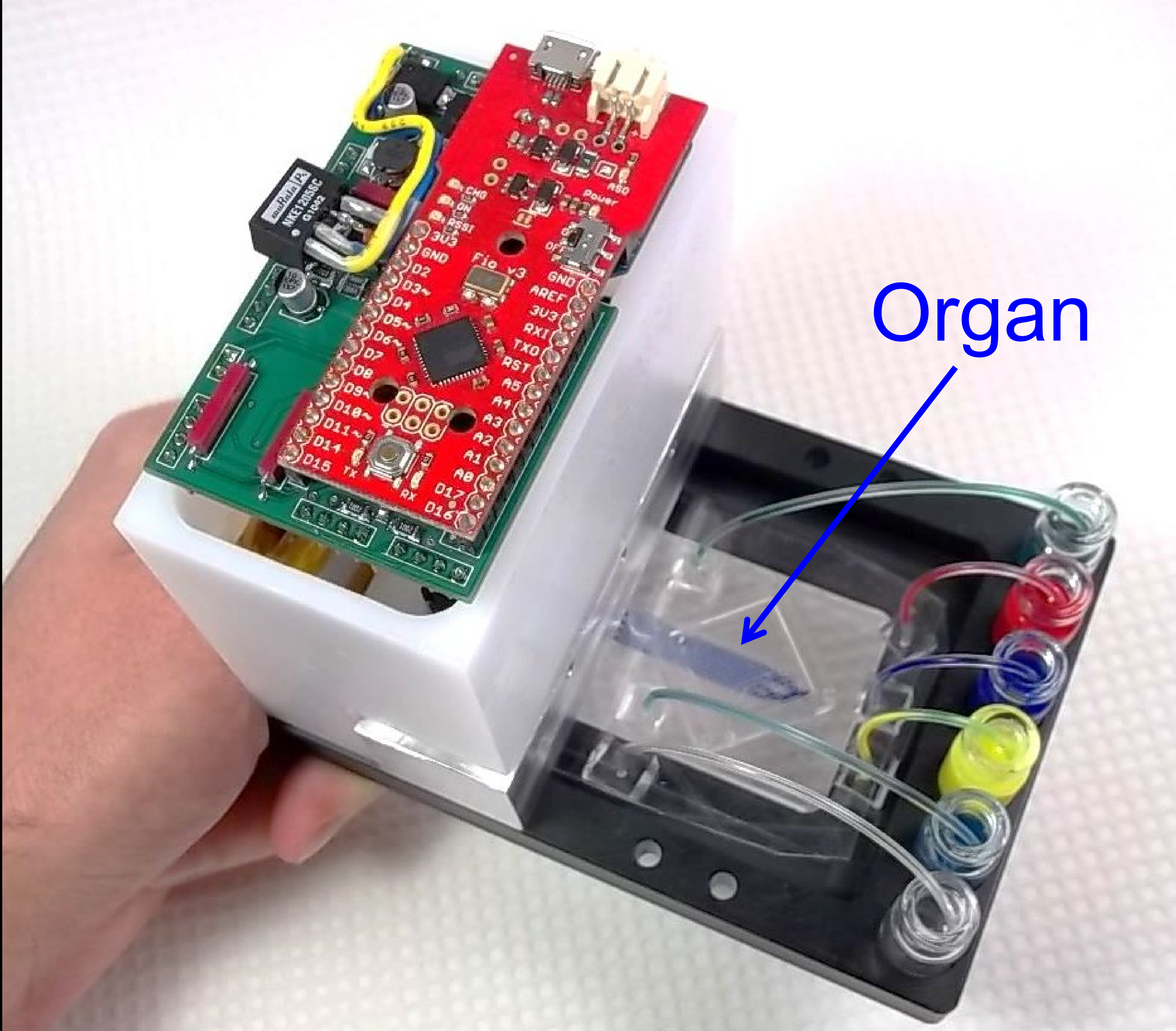
Courtesy of Kevin Seale

Brain on a chip

Simpler than a human but has the key functions of the blood-brain barrier!



Courtesy of Jackie Brown



Courtesy of Frank Block, III

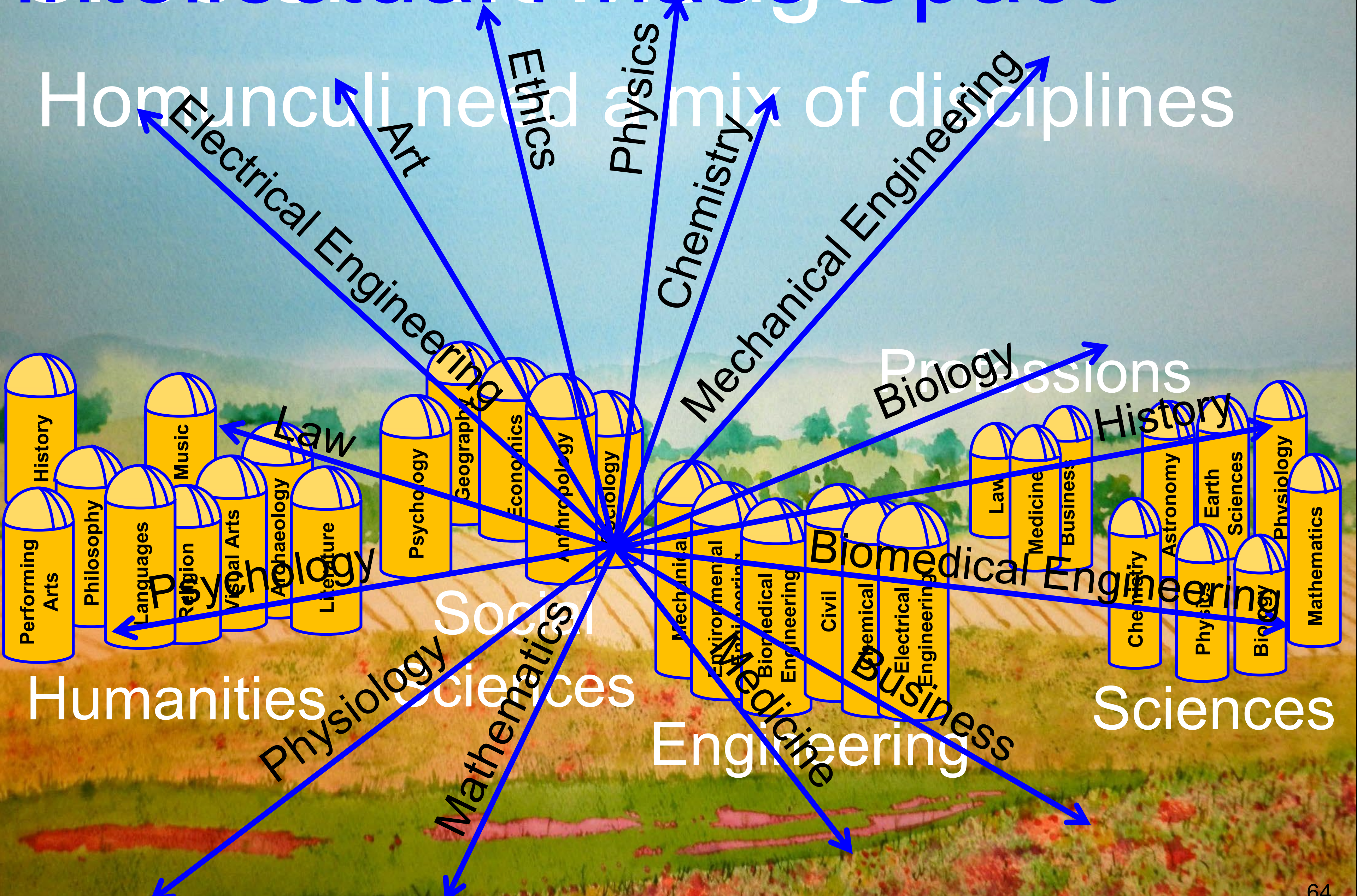
What kinds of people are building homunculi?

Fields of Knowledge

Julia Wikswo

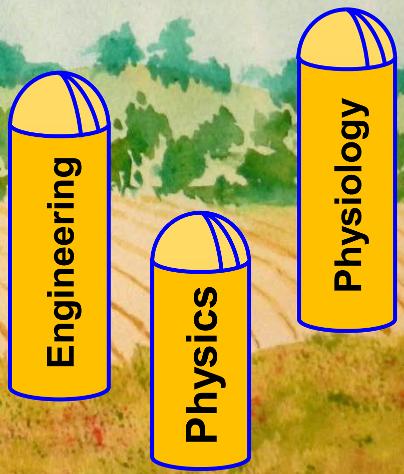
Intellectual Phase Space

Homunculi need a mix of disciplines

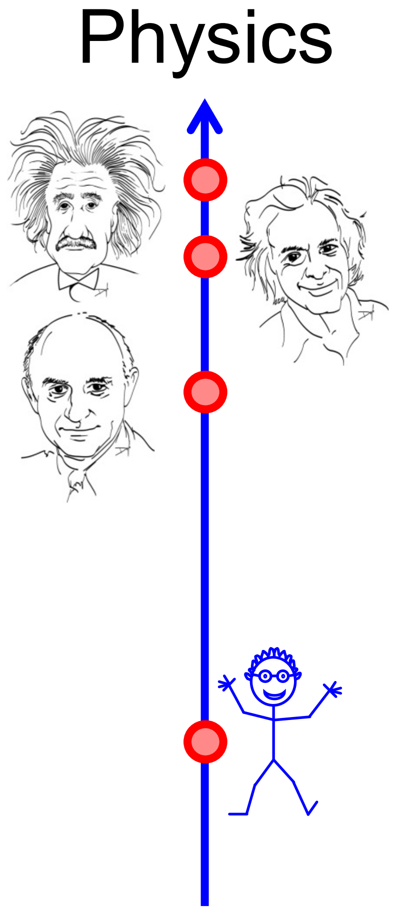


My Knowledge

You can be more than one thing at a time in phase space!

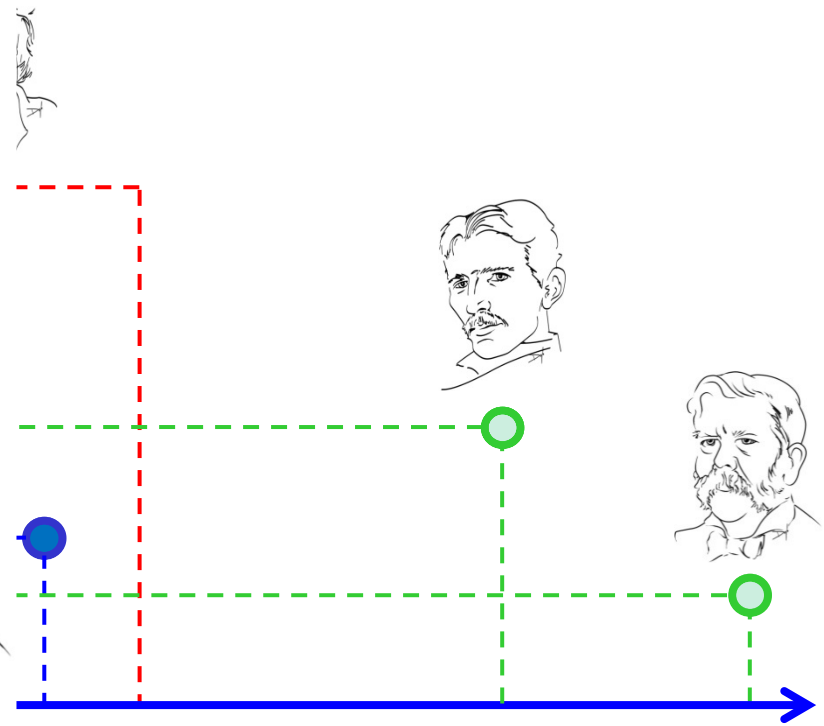


Intellectual Phase Space



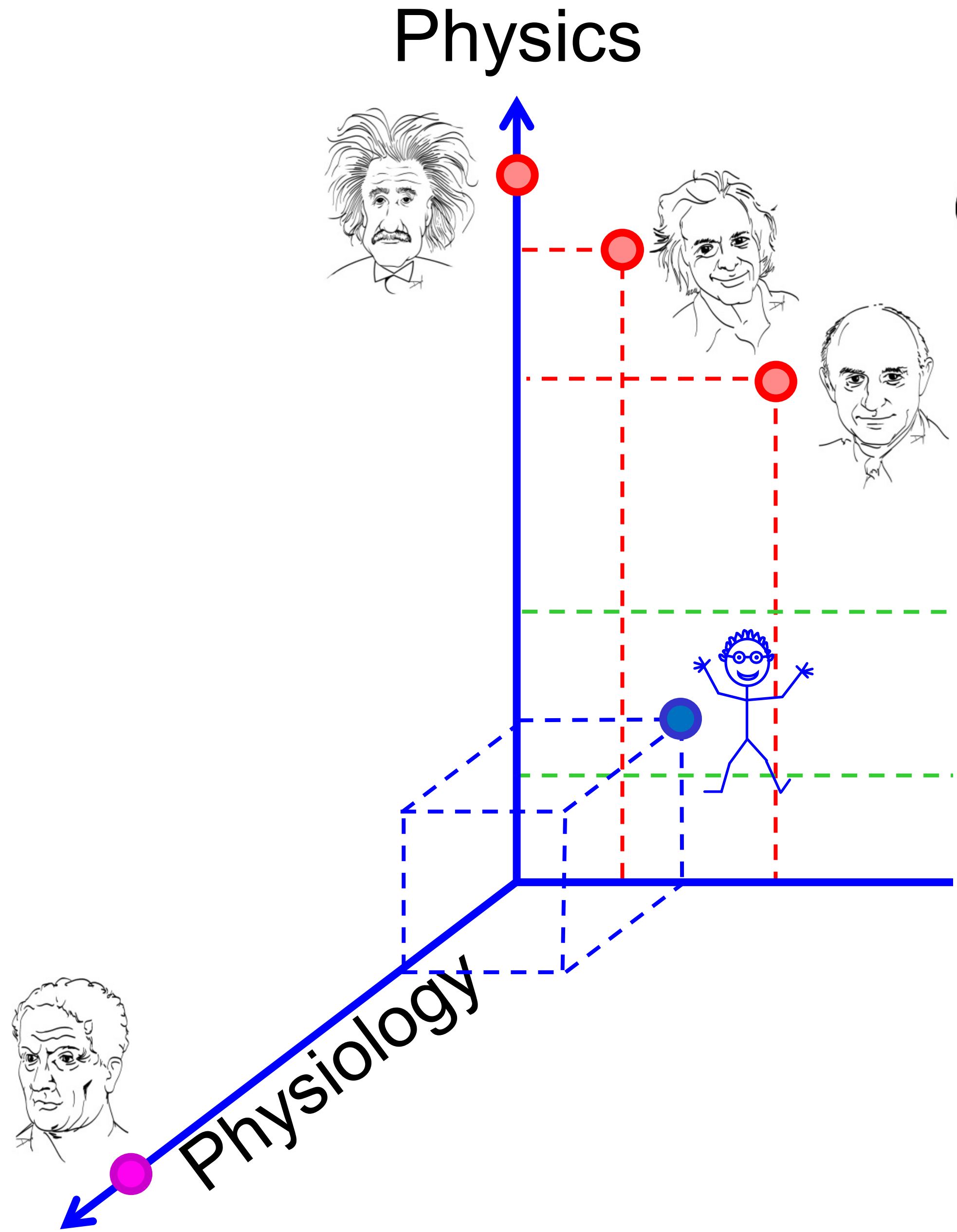
Enrico Fermi
1901-1954

Intellectual Phase Space



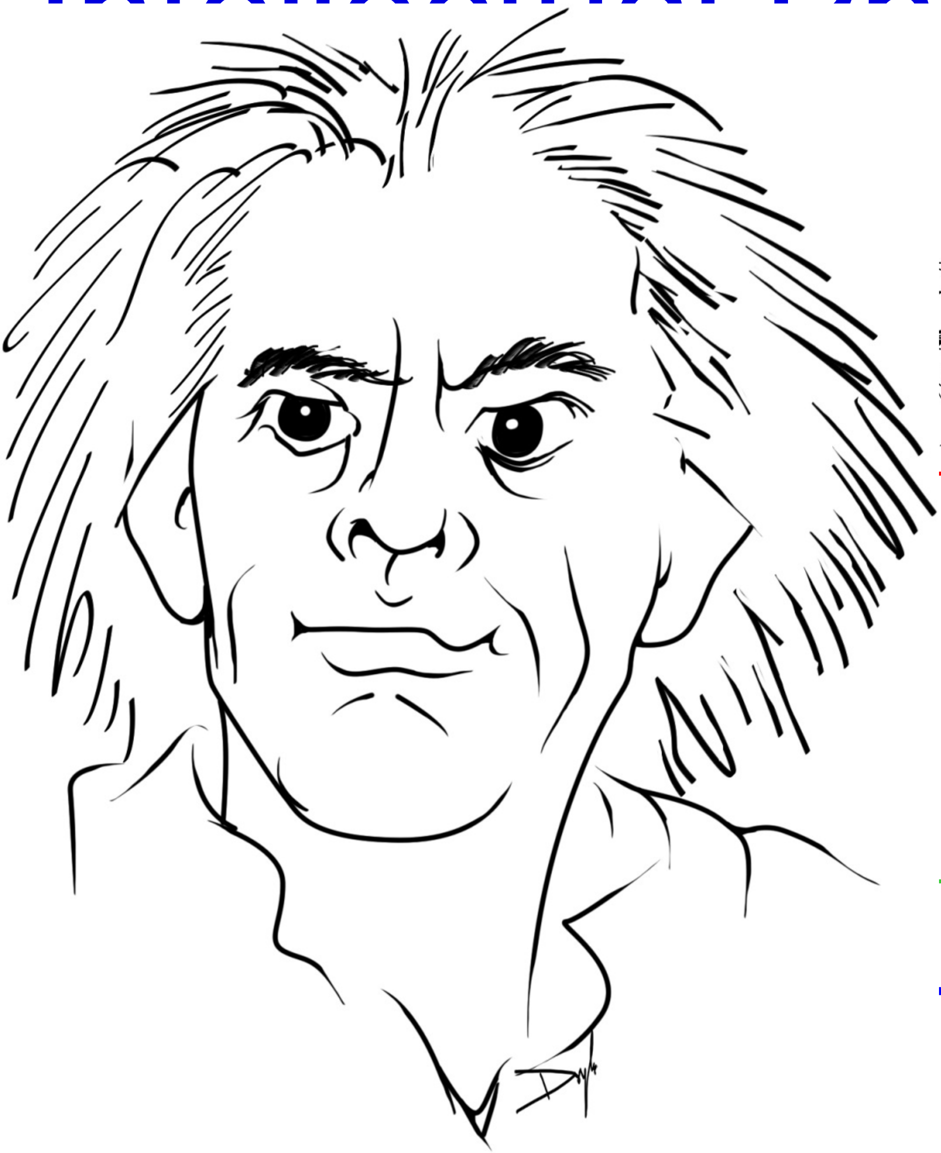
Nikola Tesla
1856-1943

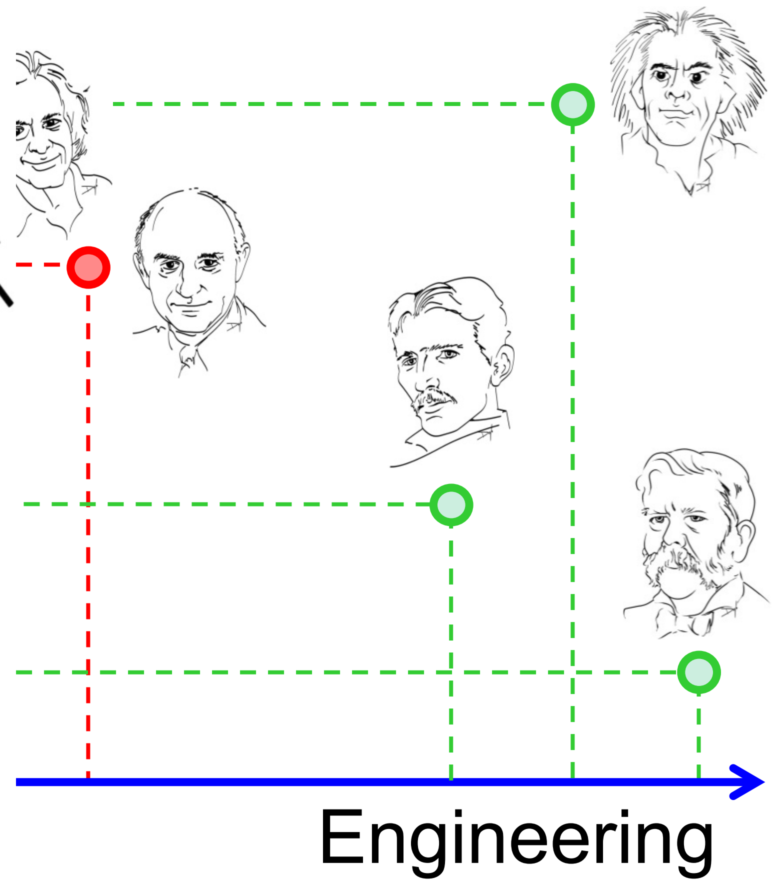
Intellectual Phase Space



Galen of Pergamon
AD 129-216

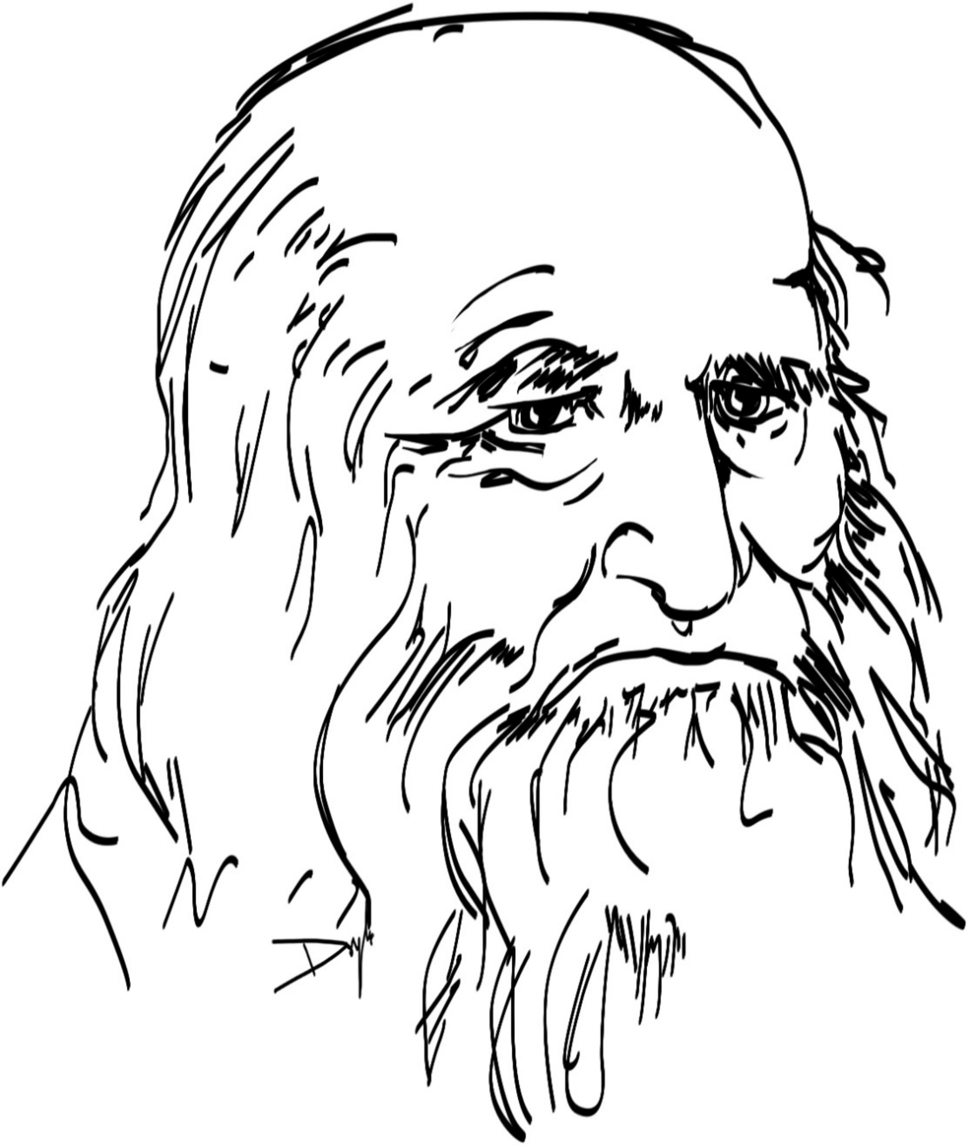
Intellectual Phase Space

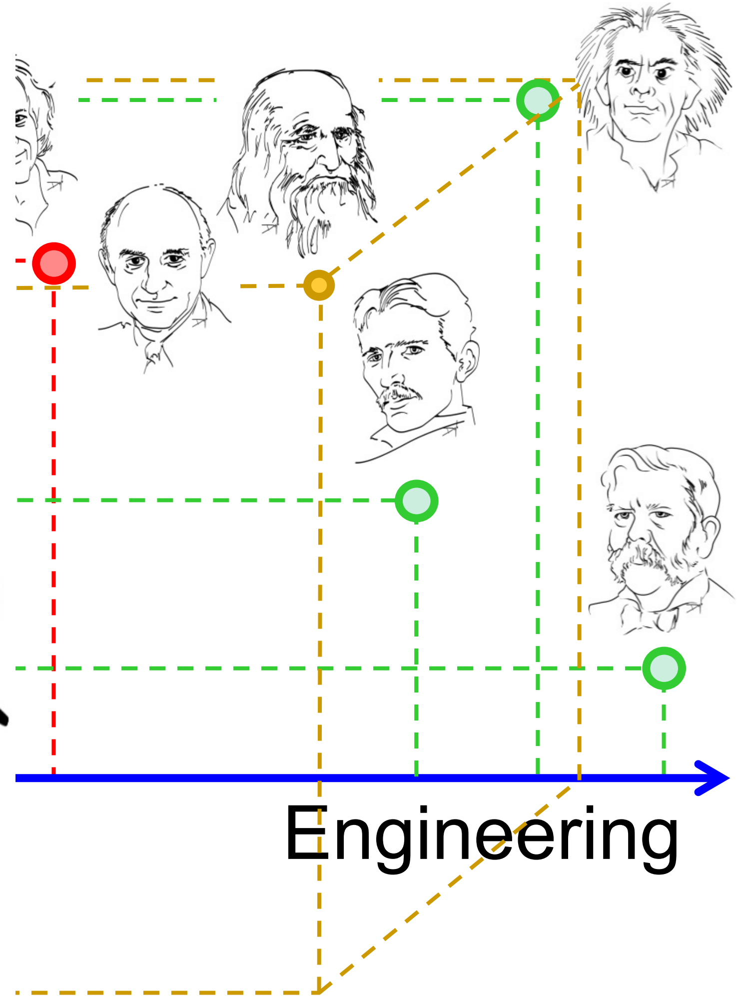




Emmett “Doc” Brown
1885-2015?

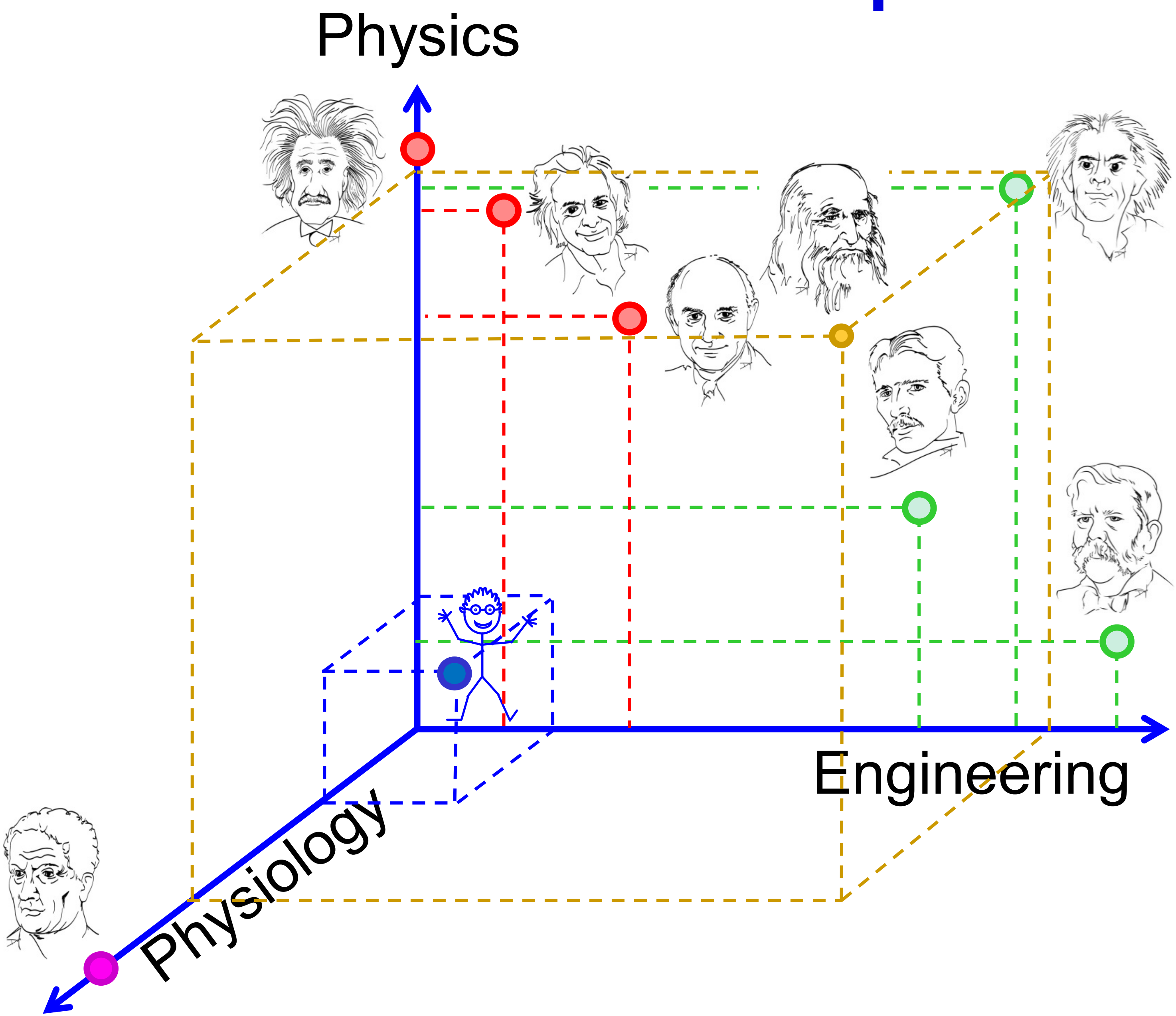
Intellectual Phase Space



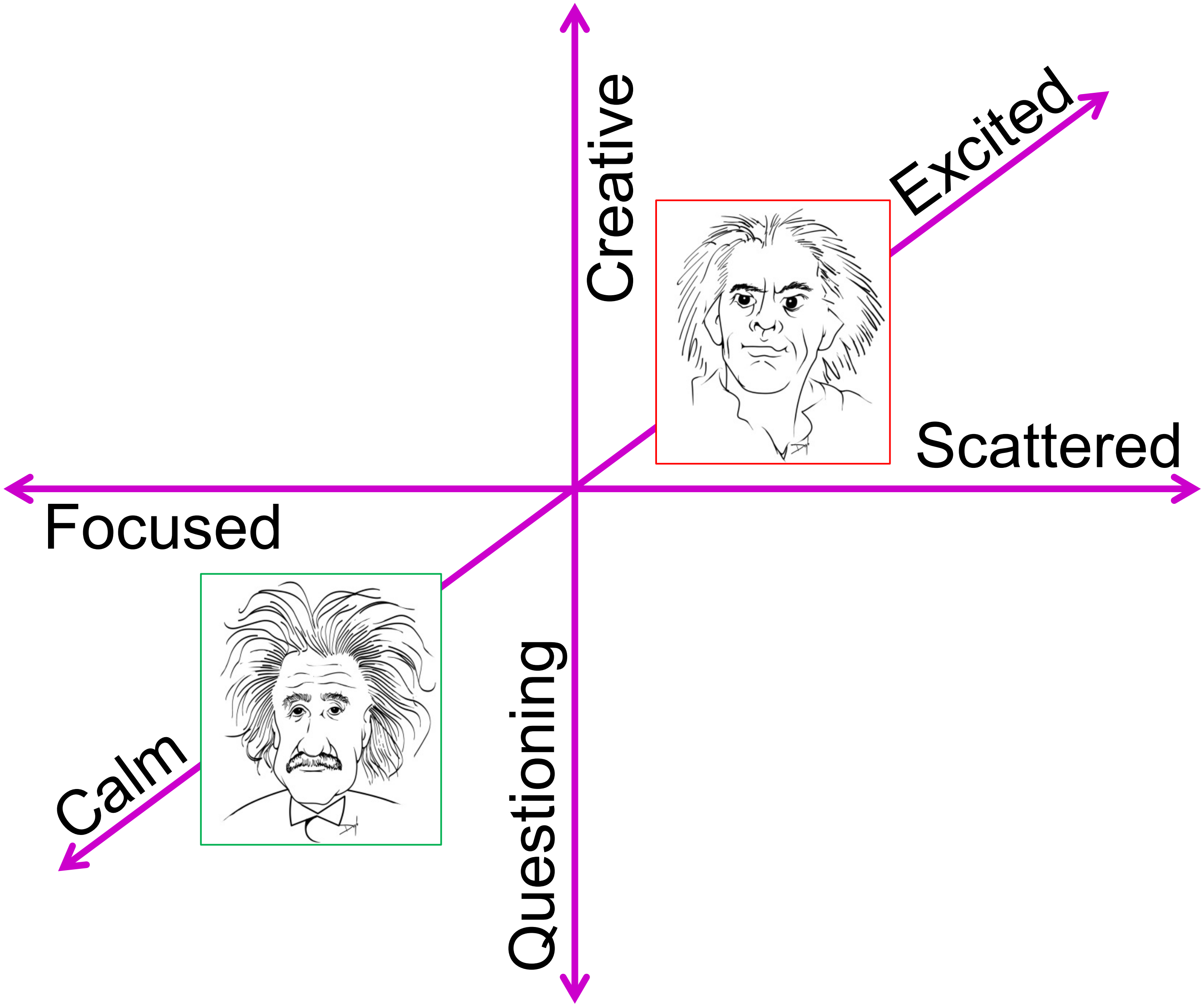


Leonardo da Vinci
1452-1519

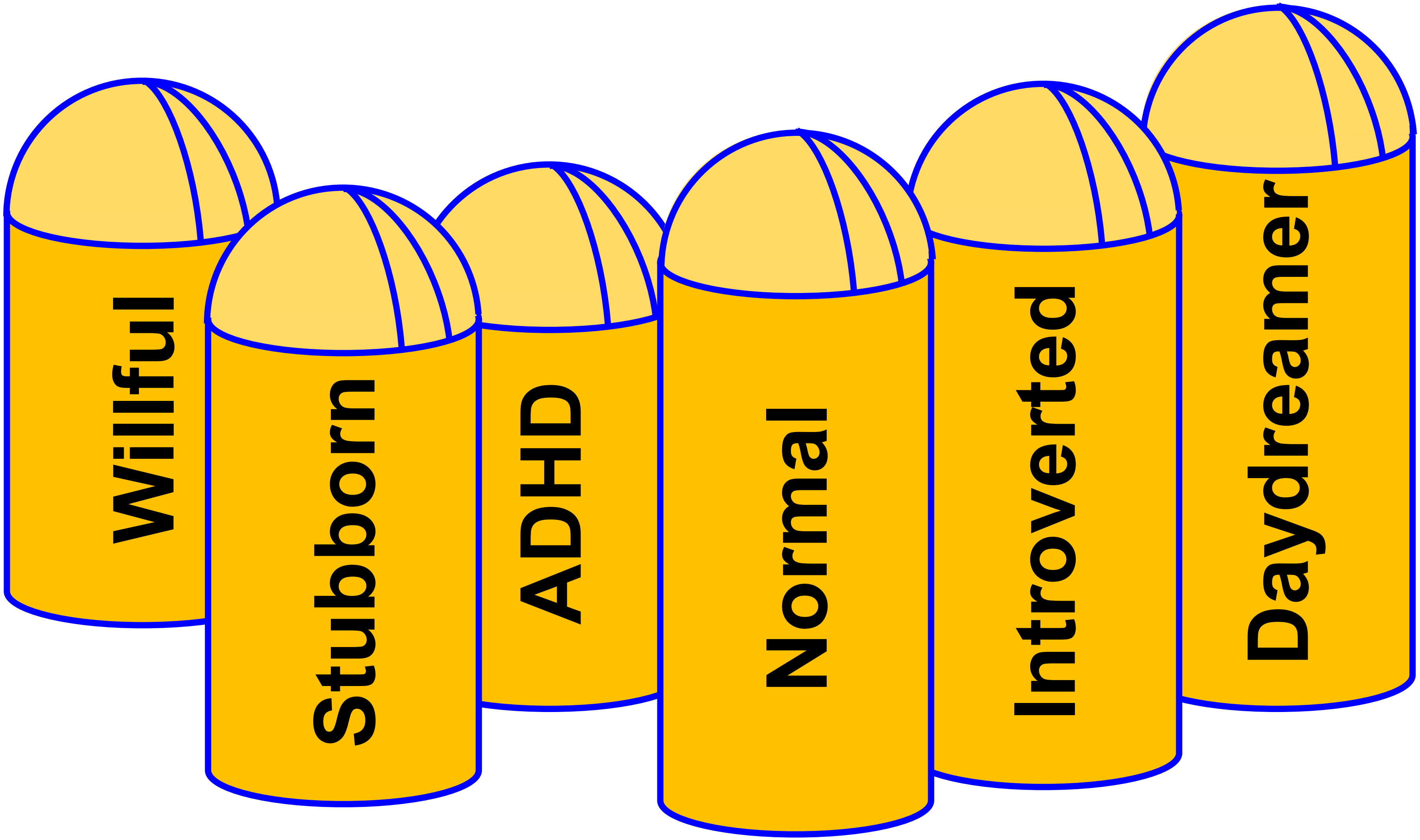
Intellectual Phase Space



Behavioral Phase Space



Behavioral Silos



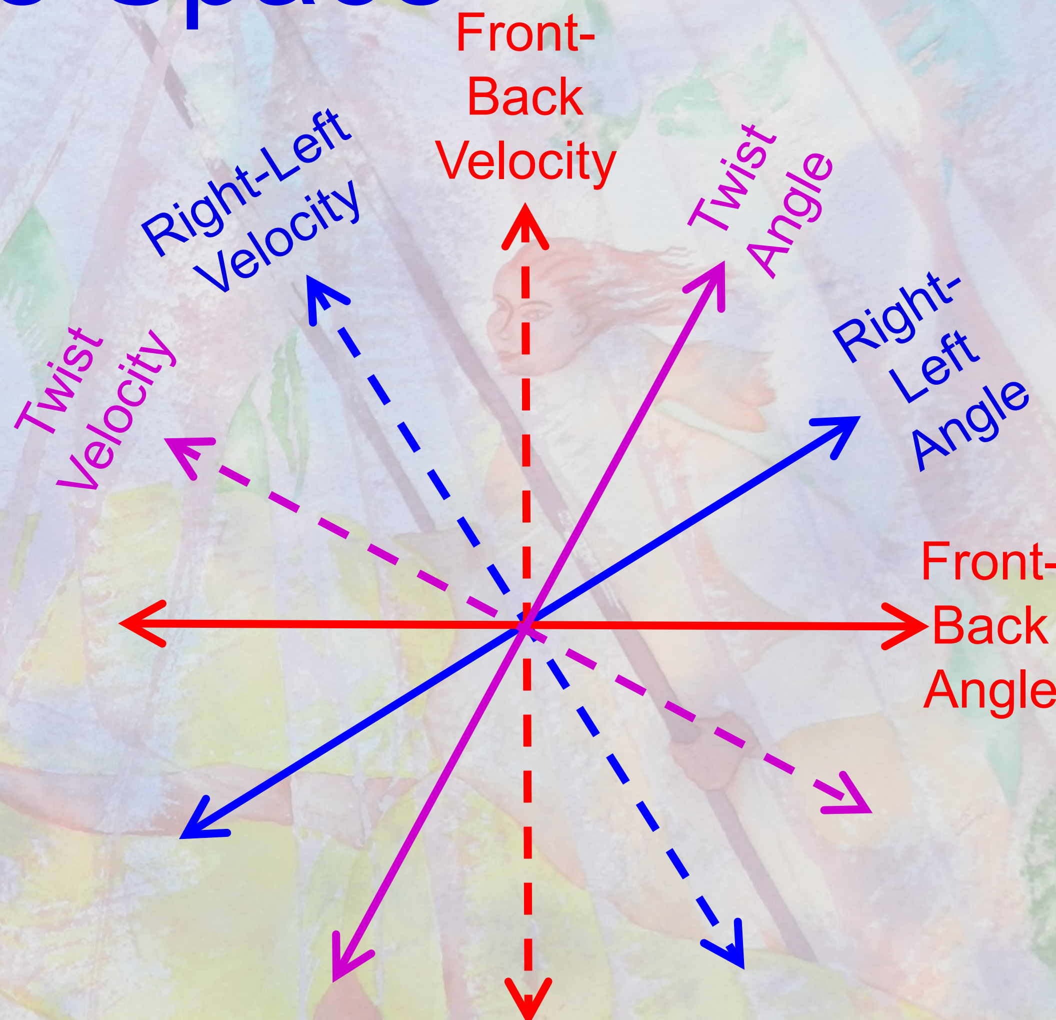
Swing Phase Space

Front and back

Left and Right

Orbit

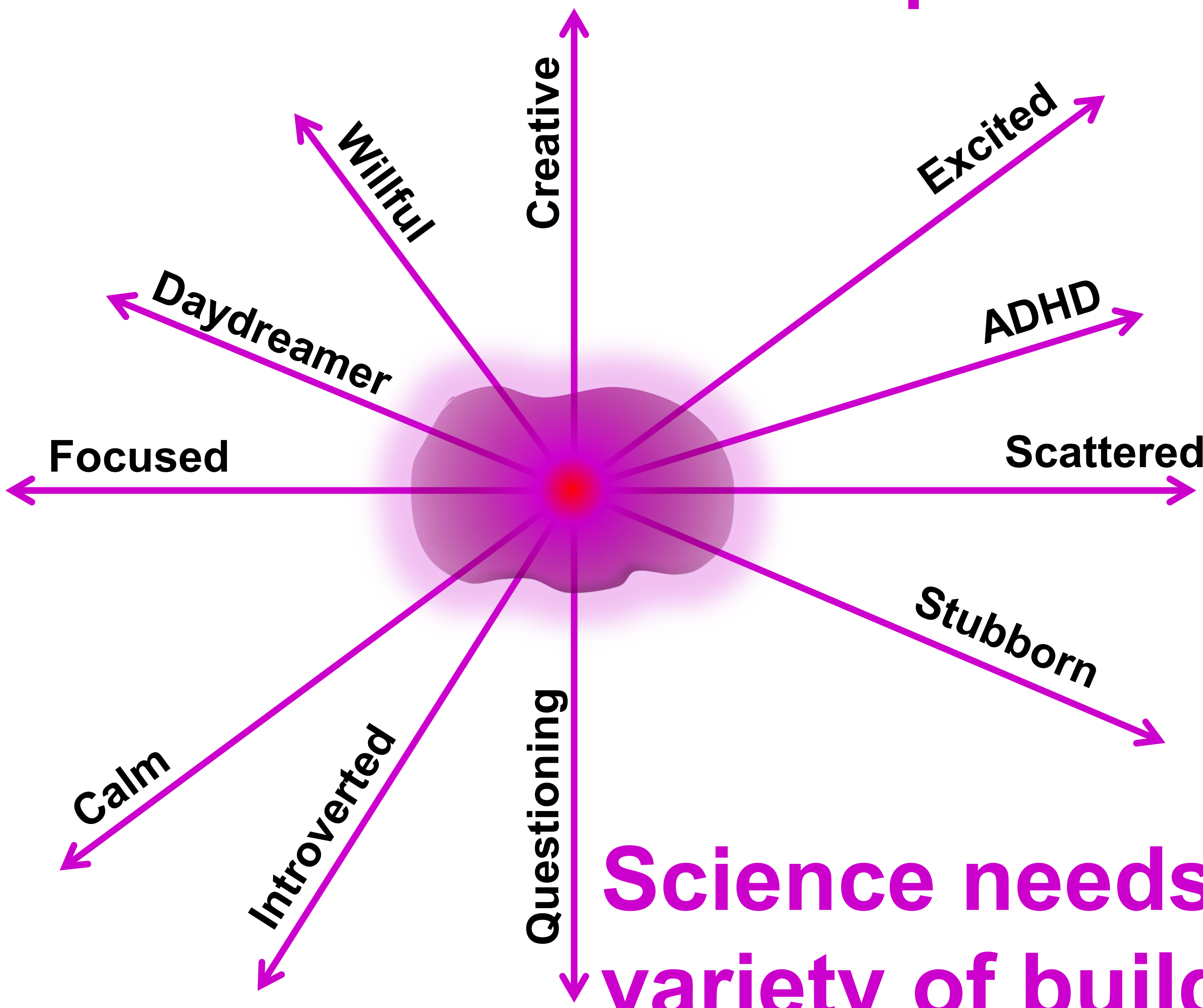
Twist



Six-Dimensional Phase Space is FUN, but often discouraged!

Don’t put people in a single silo!

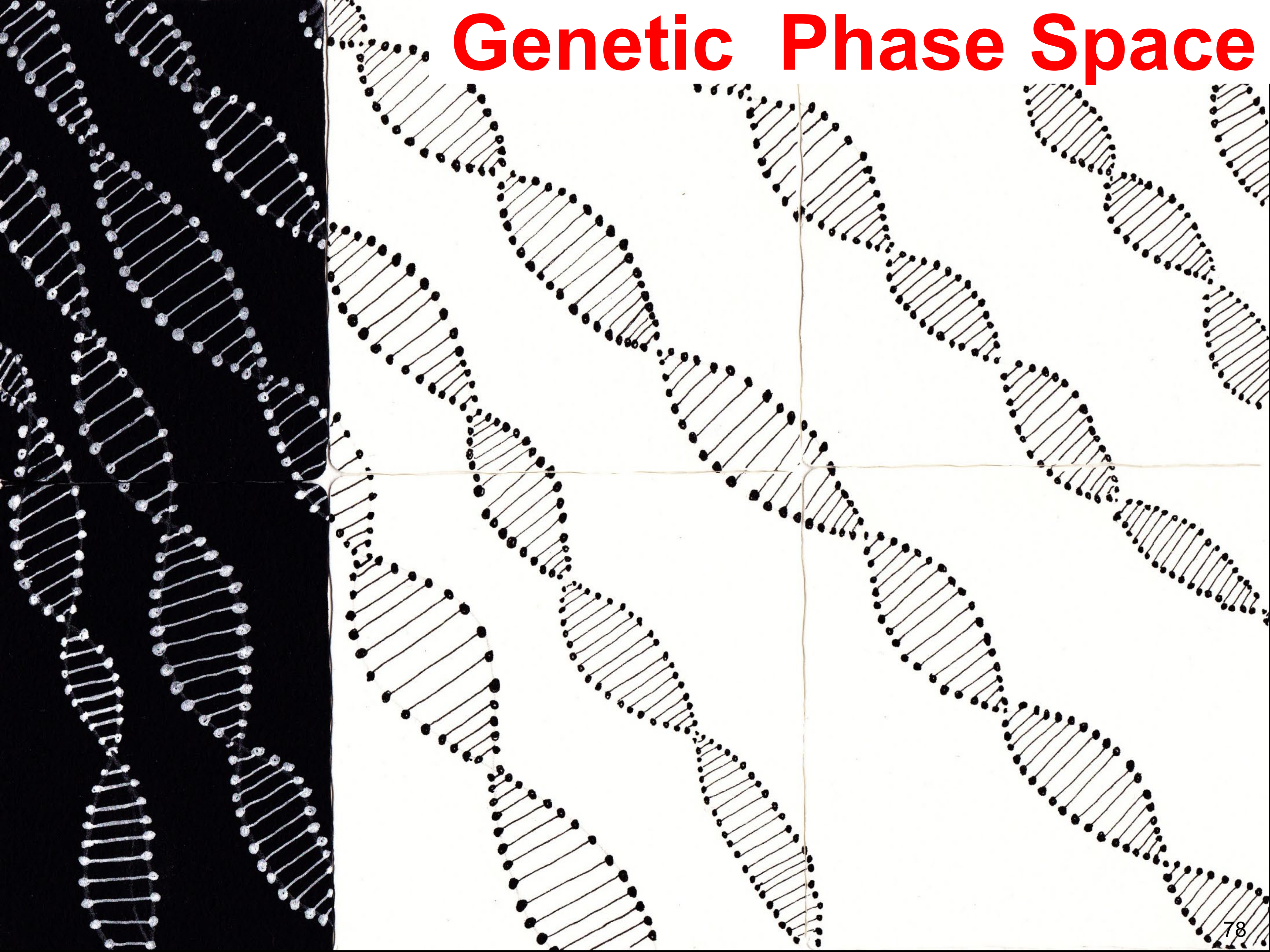
Behavioral Phase Space



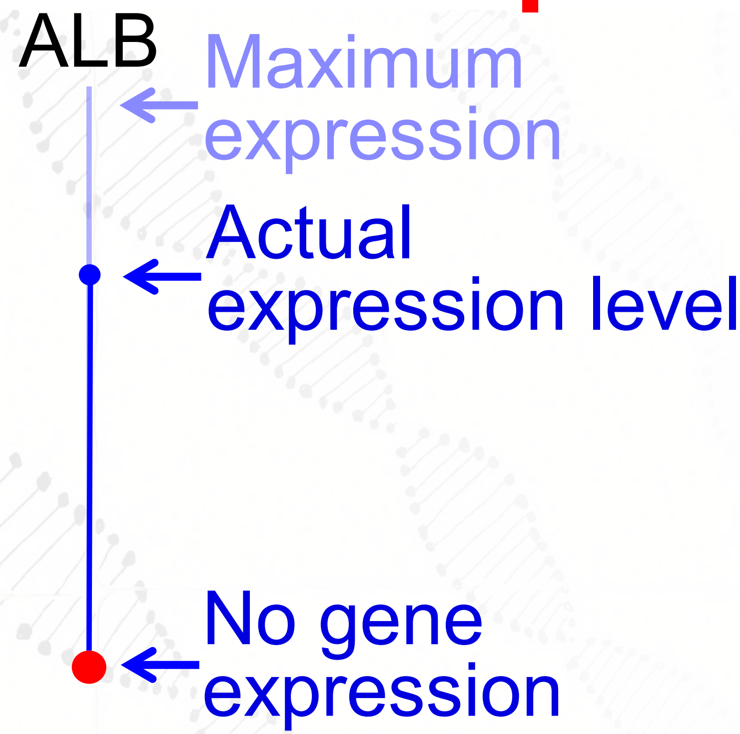
Science needs a variety of builders!

What are we learning about biology's phase space?

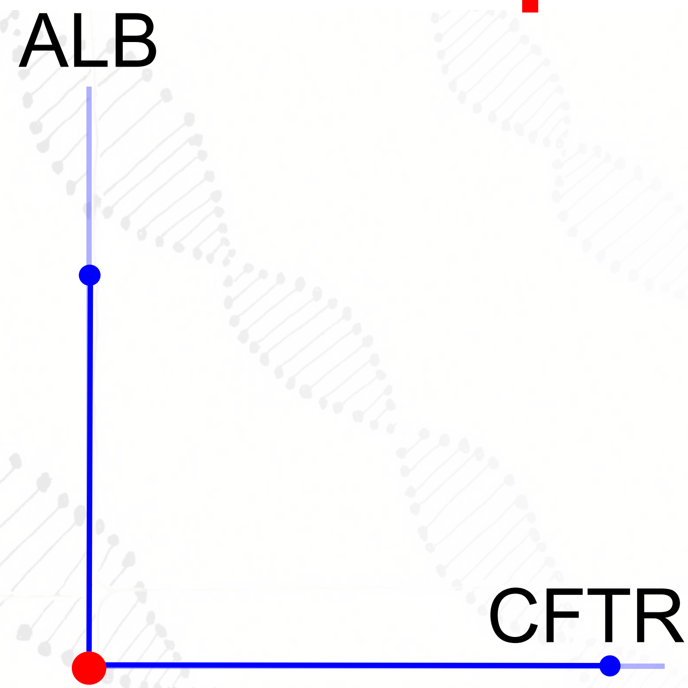
Genetic Phase Space



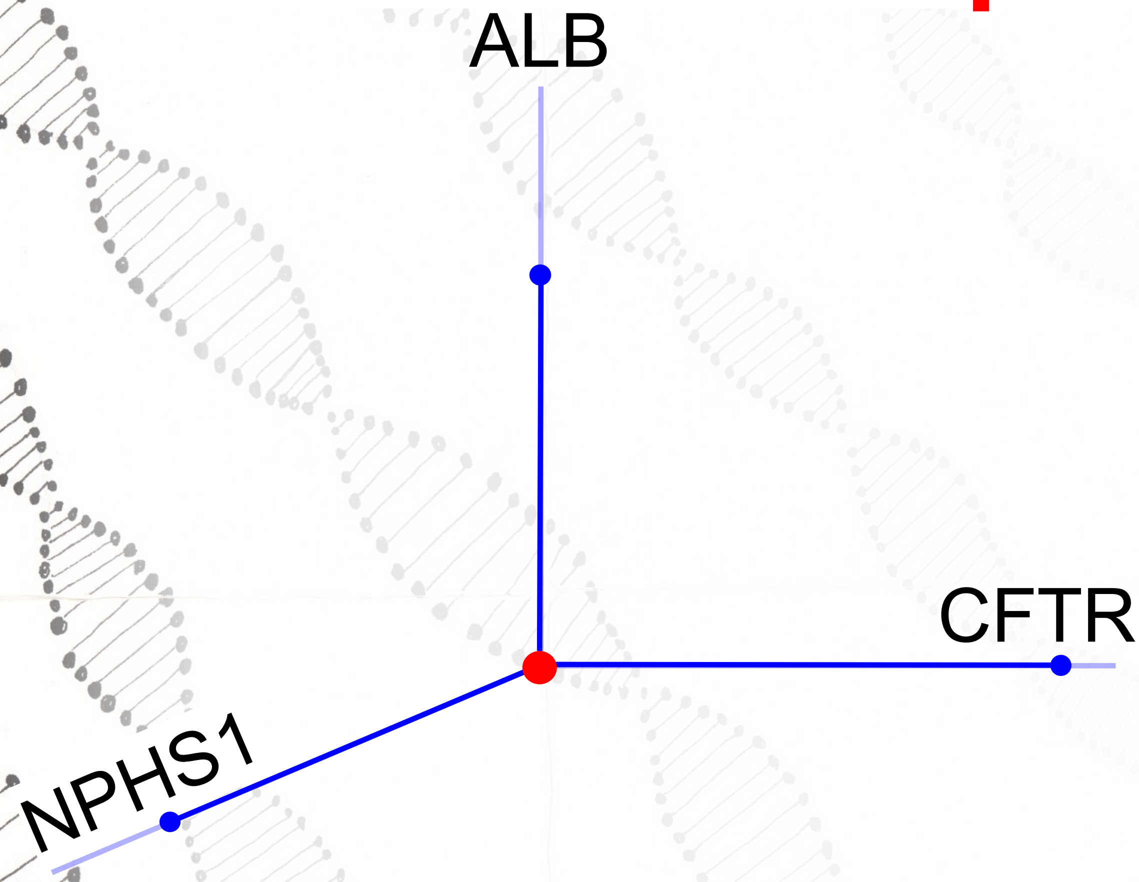
1 Gene Phase Space



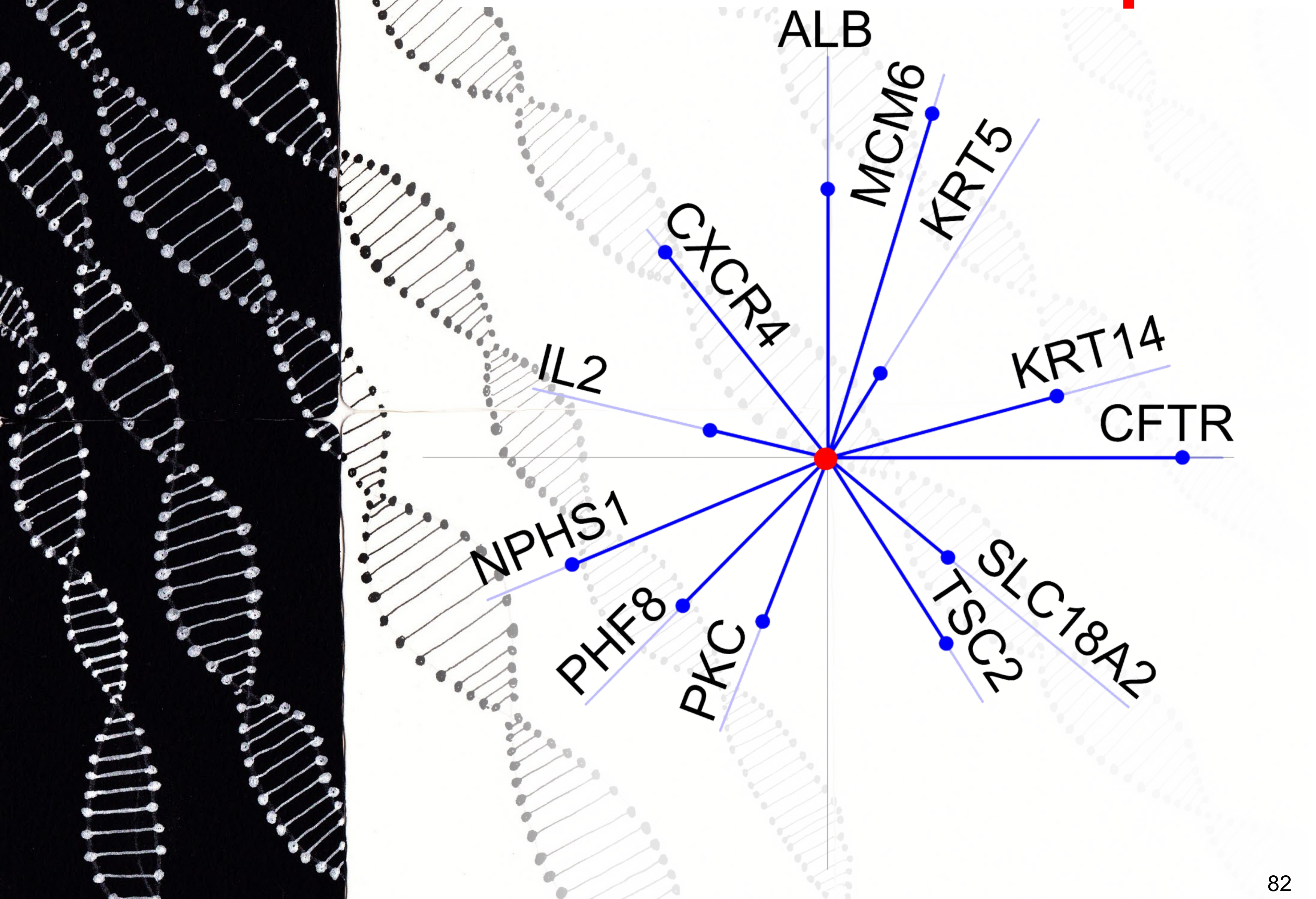
2 Gene Phase Space



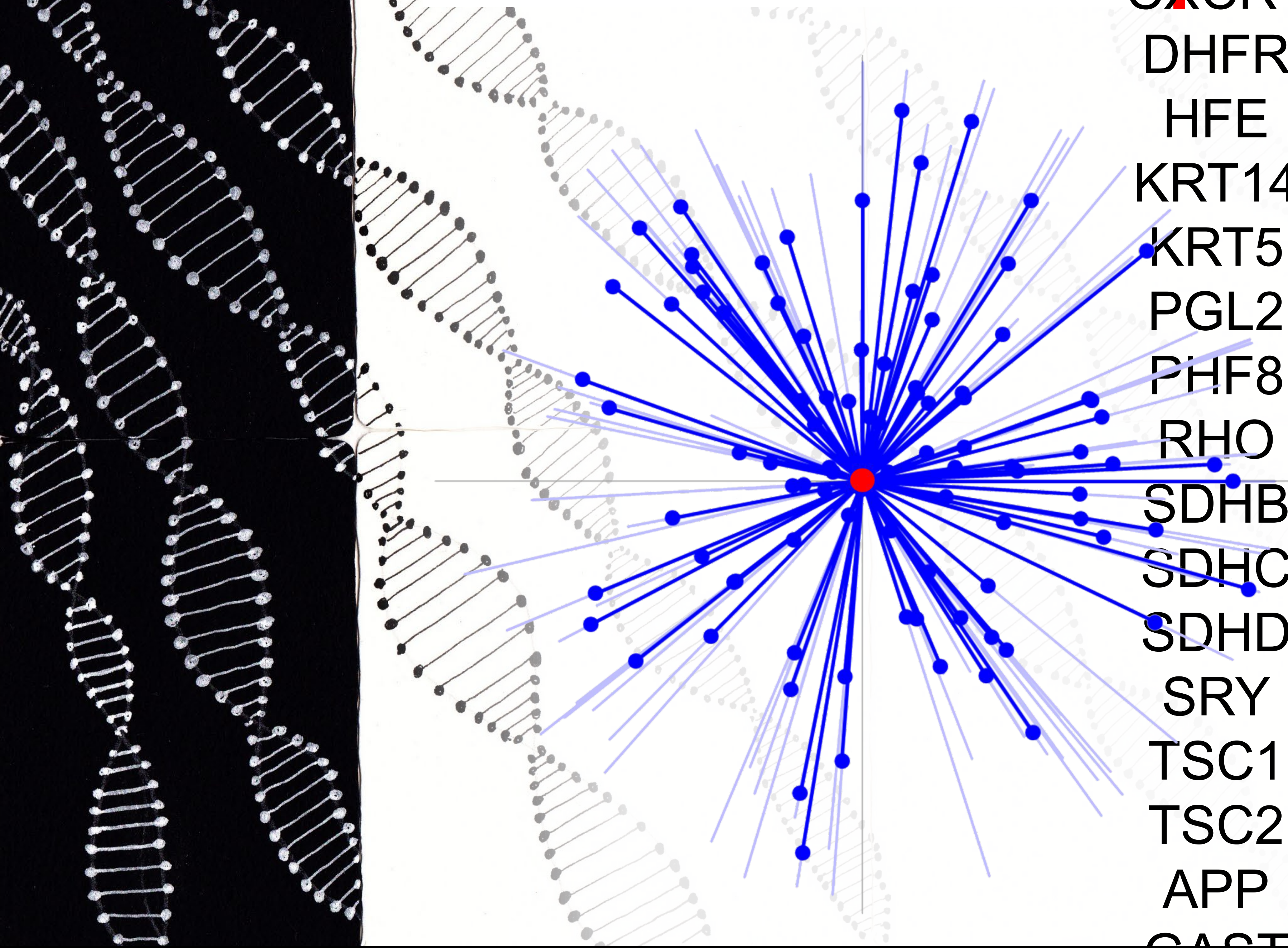
3 Gene Phase Space



12 Gene Phase Space

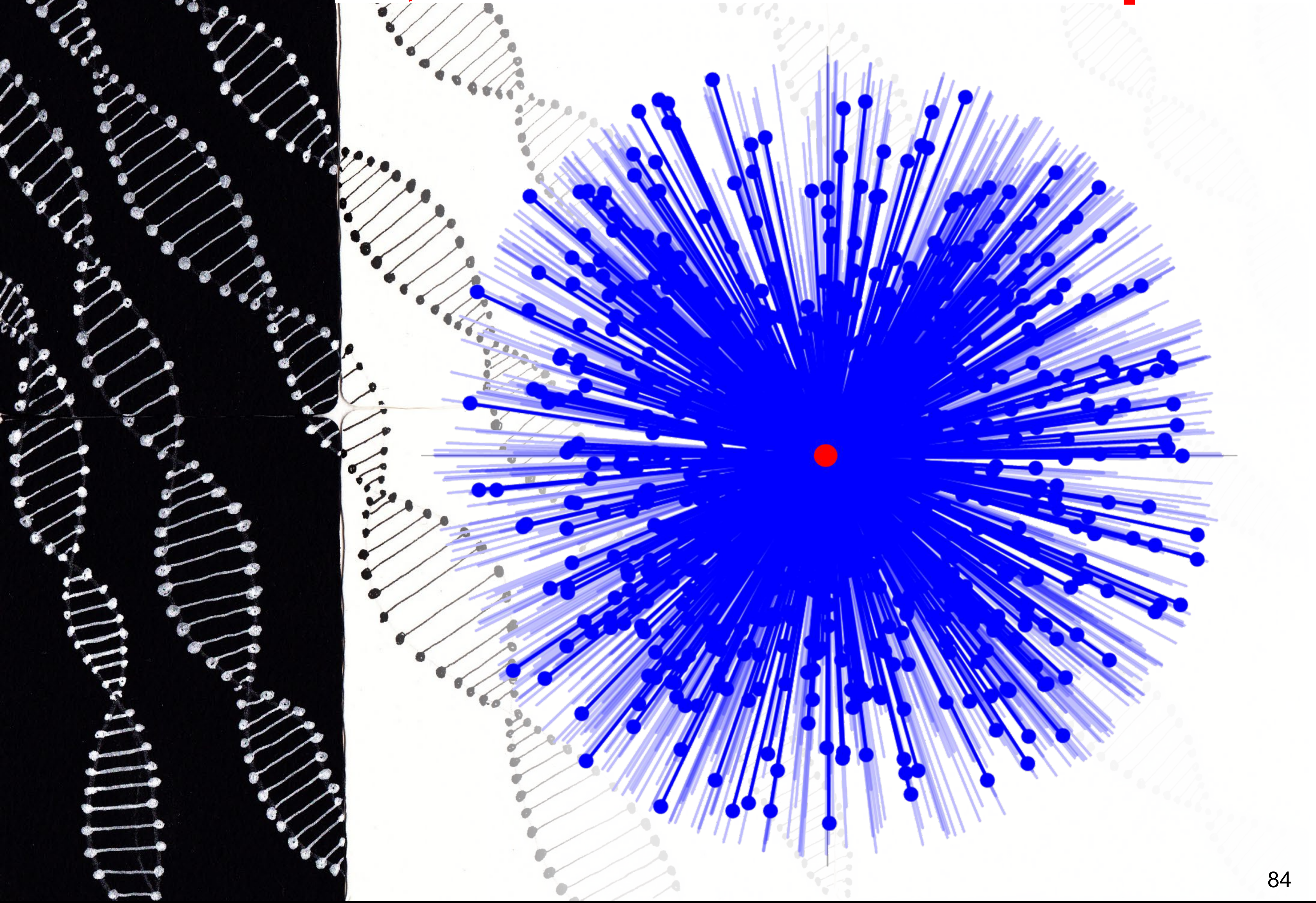


100 Gene Phase Space

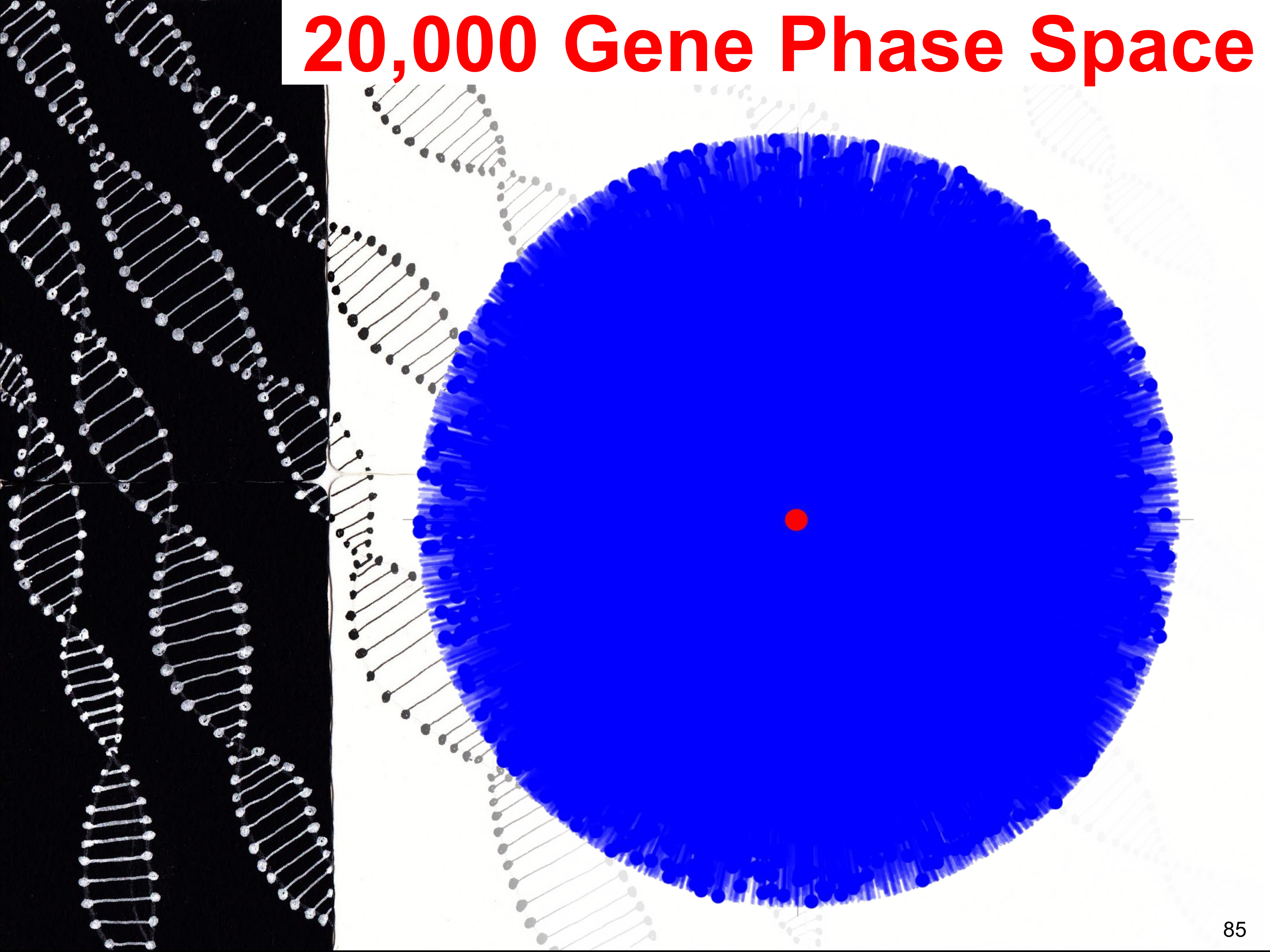


CRH
CXCR4
DHFR
HFE
KRT14
KRT5
PGL2
PHF8
RHO
SDHB
SDHC
SDHD
SRY
TSC1
TSC2
APP

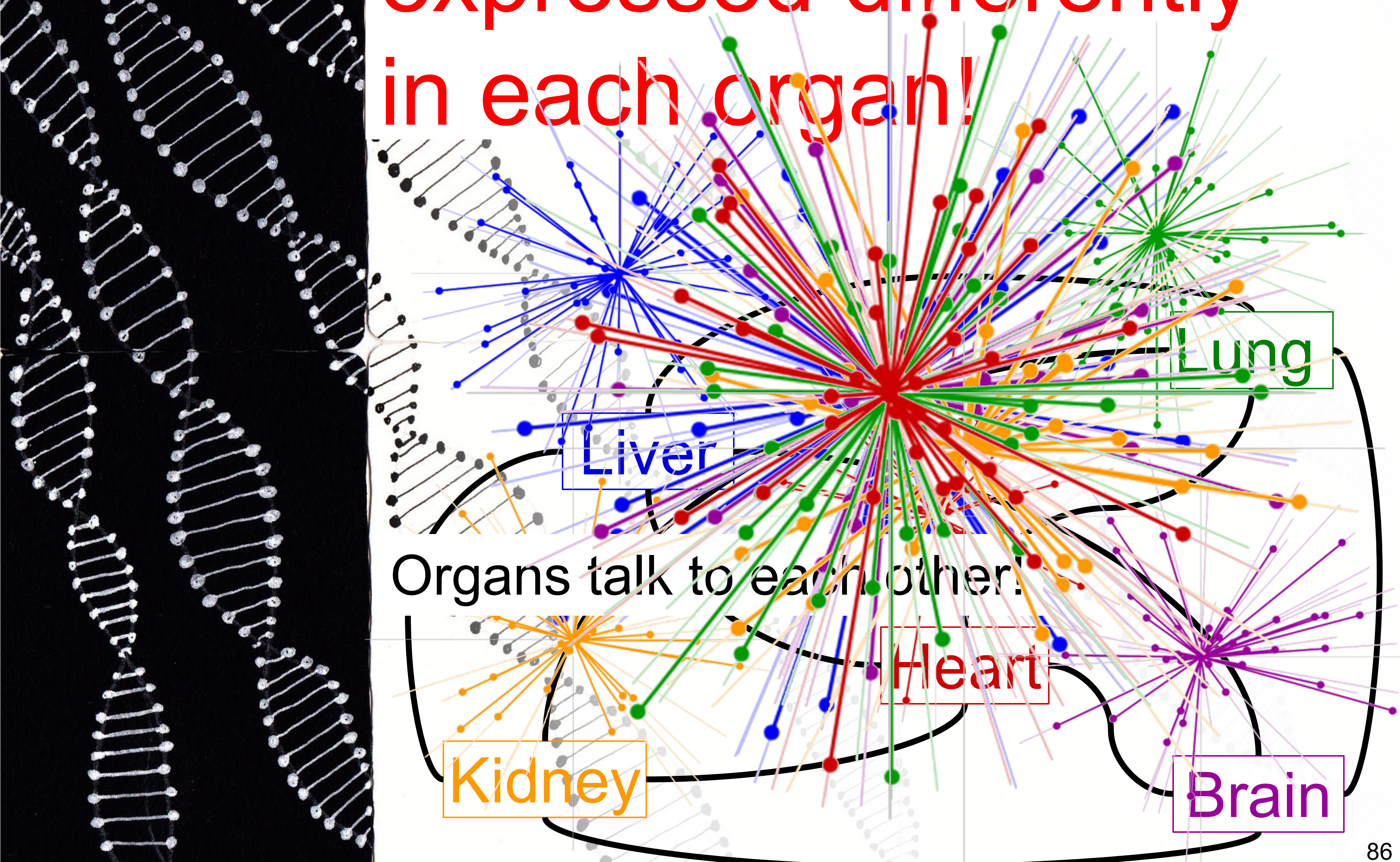
1,000 Gene Phase Space



20,000 Gene Phase Space



Our 20,000 genes are expressed differently in each organ!



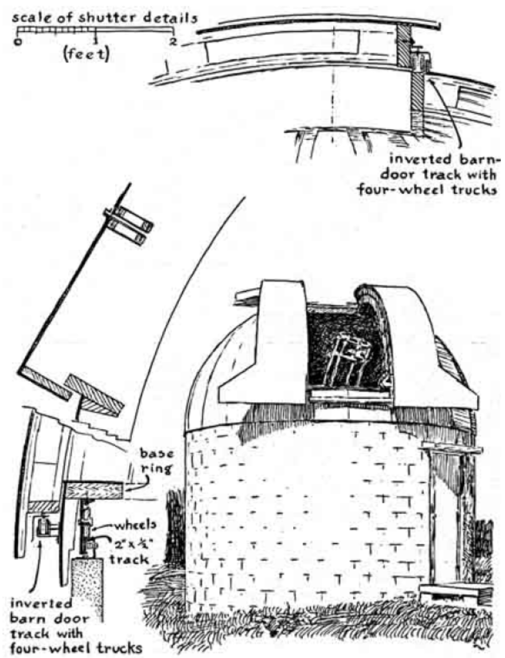
Evolution of an Interdisciplinary Career

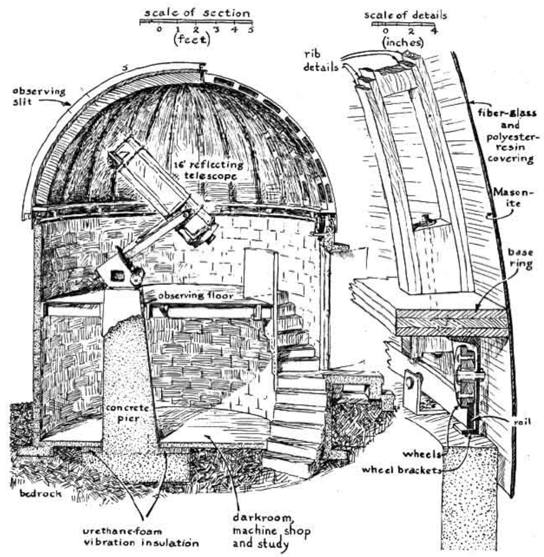
JPW Learning Timeline

1949 Born to Leonora and John Wikswo, Sr.

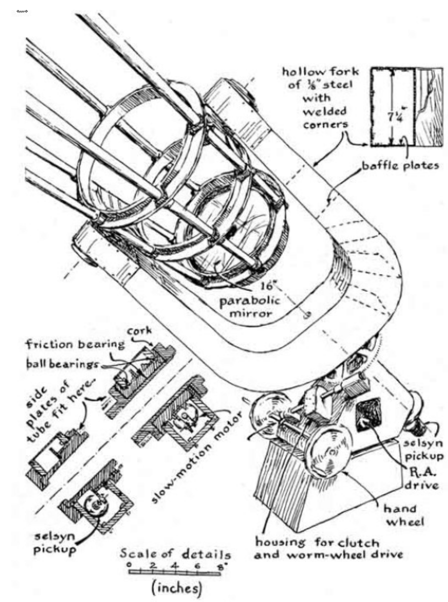
1955-1967 Apprenticed to John Wikswo, Sr.

You can learn a lot by watching stuff done right. Doing it yourself might be better.

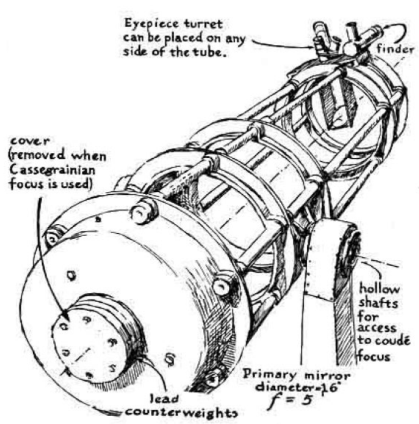




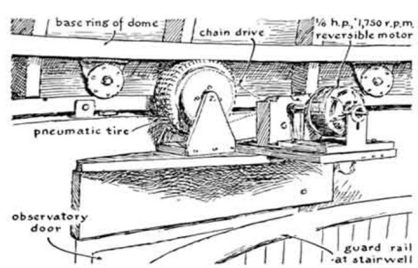
The Wikswo observatory, with details of dome at right



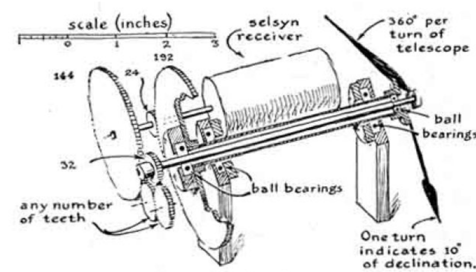
Base of the telescope mounting, with details at left



Tube of the telescope



The mechanism for rotating the dome



Readout mechanism for monitoring declination; numbers refer to gear teeth

C. L. Stong, "An Ambitious Observatory Is Built By Father and Son, The Amateur Scientist in *Scientific American,* April, 1970

JPW Learning Timeline

1949 Born to Leonora and John Wikswo, Sr.
1955-1967 Apprenticed to John Wikswo, Sr.

You can learn a lot by watching stuff done right. Doing it yourself might be better.

1965 Admitted early decision to the University of Virginia
1966 Started at UVa as an Echols Scholar (8 required courses)

Putting lots of smart students in single dorm is interesting.
Smart students can figure out what they need to learn.

1967-1970 Worked with Dr. Bascom Deaver and his graduate students

Having a skill is a foot in the door.
You learn by making, and by making mistakes.

1969-1970 Junior Fellow, UVa Society of Fellows

"How to give a mosquito an enema," Parti Québécois
Scholarly social environments can benefit learning.

1970-1975 Graduate School, Stanford

The Zen of Graduate Education: A PhD is a state of mind.

1975-1977 Postdoc, Stanford School of Medicine
1977- Joined the Vanderbilt faculty
1979 Co-founded the W.H. Sefam School

You learn quickly in a 24-7 immersion environment. Everyone learns differently.

1979 Co-sued Williamson County Superintendent of Schools and School Board

Suit Asking Recognition Of School Within Home

FRANKLIN, Tenn. — A Vanderbilt University professor and his wife, holding their children out of public school, have filed a lawsuit seeking recognition of the family school in their home.

John T. Wikswo Jr. and his wife Julia say the school they operate at their residence on Manley Lane in Brentwood is a valid private educational institution — even though their son and daughter are the only students.

WILLIAMSON COUNTY School Superintendent Ken Fleming disagrees, although he acknowledges that the law is unclear on the subject.

"The children need to be in school somewhere, either in a public or a private school," Fleming said yesterday.

The Wikswo youngsters, Mathew and Sarah, were enrolled at Scales Elementary School in Brentwood during 1978-79, one in the first grade and the other in the second, Fleming said.

LAST SEMESTER, though, the children were kept at home, their parents saying they were being educated in the "W.H. Sefam School." In their Chancery Court lawsuit, the parents list Wikswo as director of the school and his wife as a teacher.

Both Wikswo, an assistant professor of physics and astronomy at Vanderbilt, and his wife declined to discuss any aspect of the matter yesterday.

The suit, filed on their behalf by Nashville attorneys John C. Tune and Ben C. Fordham, seeks a declaratory judgment on the validity of W.H. Sefam School.

FLEMING SAID he sent a team of county school supervisors to the Wikswo home about a month ago, then held a discussion of the situation in his office.

(Turn to Page 16, Column 1)

Suit Asking Recognition Of School Within Home

FRANKLIN, Tenn. — A Vanderbilt University professor and his wife, holding their children out of public school, have filed a lawsuit seeking recognition of the family school in their home.

John T. Wikswo Jr. and his wife Julia say the school they operate at their residence on Manley Lane in Brentwood is a valid private educational institution — even though their son and daughter are the only students.

WILLIAMSON COUNTY School Superintendent Ken Fleming disagrees, although he acknowledges that the law is unclear on the subject.

"The children need to be in school somewhere, either in a public or a private school," Fleming said yesterday.

The Wikswo youngsters, Mathew and Sarah, were enrolled at Scales Elementary School in Brentwood during 1978-79, one in the first grade and the other in the second, Fleming said.

LAST SEMESTER, though, the children were kept at home, their parents saying they were being educated in the "W.H. Sefam School." In their Chancery Court lawsuit, the parents list Wikswo as director of the school and his wife as a teacher.

Both Wikswo, an assistant professor of physics and astronomy at Vanderbilt, and his wife declined to discuss any aspect of the matter yesterday.

The suit, filed on their behalf by Nashville attorneys John C. Tune and Ben C. Fordham, seeks a declaratory judgment on the validity of W.H. Sefam School.

FLEMING SAID he sent a team of county school supervisors to the Wikswo home about a month ago, then held a discussion of the situation in his office.

(Turn to Page 16, Column 1)

The Tennessean 1-6-80

VU Professor, Wife Seek Home-School Recognition

(Continued From Page One)

"It seemed to us it was really just home instruction, and wouldn't fit what anybody would call a school," the superintendent said.

"I really feel like kids need that early exposure to society," he said.

FLEMING SAID no immediate action was taken to force the couple to place the children in a recognized school, because he felt "the persuasion route" was a better approach.

State law requires that children of ages 7 through 16 attend either a public or private school. However, the law does not define a private school, Fleming said.

"While I regret that it was our school system that had to be involved," he said, "I do think it is a legal question to which there needs to be an answer, whatever the answer is, and a court is where it will have to be answered."

ACCORDING TO officials of the state Department of Education, the case apparently has no precedent in Tennessee.

Similar cases have been heard in other states, with court decisions varying from one state to another, Fleming noted.

"Religion is an issue frequently in other states, but religion doesn't appear to be a factor in this case," he said.

FLEMING SAID the Wikswos have indicated that they would rather enroll their children in a public school than in a private school other than their own.

"They're really nice people," the superintendent said, adding that he feels the couple's move for a declaratory judgment was a "constructive approach" to the matter.

The lawsuit names as defendants Fleming and the members of the Williamson County School Board.

"THE SCHOOL board hasn't really dealt with this," Fleming said. "They're being sued about it, but that's their only involvement."

The defendants have 30 days in which to respond to the suit, but Fleming said they may have to request an extension since County Attorney Rick Buerger is ill.

JPW Learning Timeline

1949 Born to Leonora and John Wikswo, Sr.
1955-1967 Apprenticed to John Wikswo, Sr.
You can learn a lot by watching stuff done right. Doing it yourself might be better.
1965 Admitted early decision to the University of Virginia
1966 Started at UVa as an Echols Scholar (8 required courses)
Putting lots of smart students in single dorm is interesting.
Smart students can figure out what they need to learn.
1967-1970 Worked with Dr. Bascom Deaver and his graduate students
Having a skill is a foot in the door.
You learn by making, and by making mistakes.
1969-1970 Junior Fellow, UVa Society of Fellows
"How to give a mosquito an enema," Parti Québécois
Scholarly social environments can benefit learning.
1970-1975 Graduate School, Stanford
The Zen of Graduate Education: A PhD is a state of mind.
1975-1977 Postdoc, Stanford School of Medicine
1977- Joined the Vanderbilt faculty
1979 Co-founded the W.H. Sefam School
You learn quickly in a 24-7 immersion environment. Everyone learns differently.
1979 Co-sued Williamson County Superintendent of Schools and School Board
Learning without boxes scares some people.
1983 Proposed the College Scholars Program
Outstanding students need outstanding classes, not boxes to check.
1987 Taught one of the first College Scholars Seminars
Revolutions in Physics, How Things Work, What is Life? Origins of Life, The Microbiome

Revolutions in Physics - 1987

VANDERBILT UNIVERSITY

INTER-OFFICE CORRESPONDENCE

Date: January 6, 1987

To: David Tuleen, Associate Dean, College of Arts & Science

From: John P. Wikswo, Dept. of Physics & Astronomy John

Subject: VAX Computer Account for College Honors 182

As you know, I'll be teaching College Honors 182, a seminar entitled "Revolutions in Physics", for the first time this semester. Since it is a seminar, it is crucial to incorporate student feedback and questions as quickly as possible after each class meting. For this reason, I would like to have you provide each of the students in this class a small account on the new VAX 8800, so that they can send me by electronic mail their biweekly responses to my solicitation for questions and comments. While I realize that the economics of the DEC 10 are more favorable to the College, the service provided by this machine is completely unacceptable, and the DEC 10 will become virtually unavailable after spring break. While I do not know how much money should be allocated to each student's account, I expect the bare minimum should suffice. I will indicate to the students that these funds are not provided for word processing or games, but solely for electronic mail. I will also tell them that over expenditures of their account will require a detailed explanation by them to you. You might check with Dean Venable as to the appropriate size for this allocation.

Since we do not yet have the class roll for this course, I would like you to authorize me to take the roll, when I receive it, directly to the Computer Center to initiate the accounts. Could you please provide me with the appropriate information.

Thank you very much for your help with this matter.

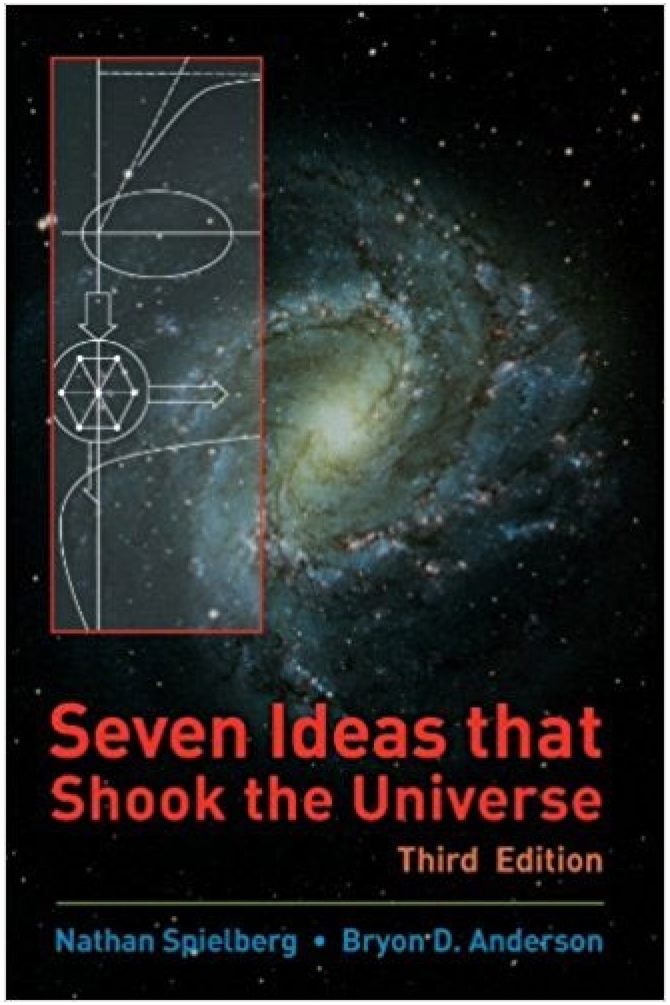
JPW/cdc

xc: George Graham, Associate Dean, College of Arts & Science

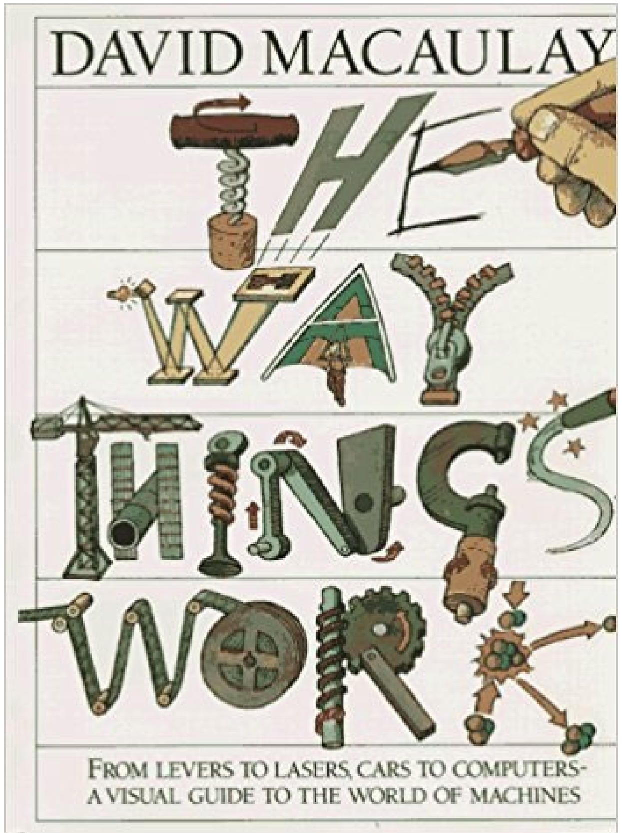
… Since it is a seminar, it is crucial to incorporate student feedback and questions as quickly as possible after each class meeting. I would like to have you provide each of the students in this class a small account on the new VAX 8800, so that they can send me by electronic mail their biweekly responses to my solicitation for questions and comments.

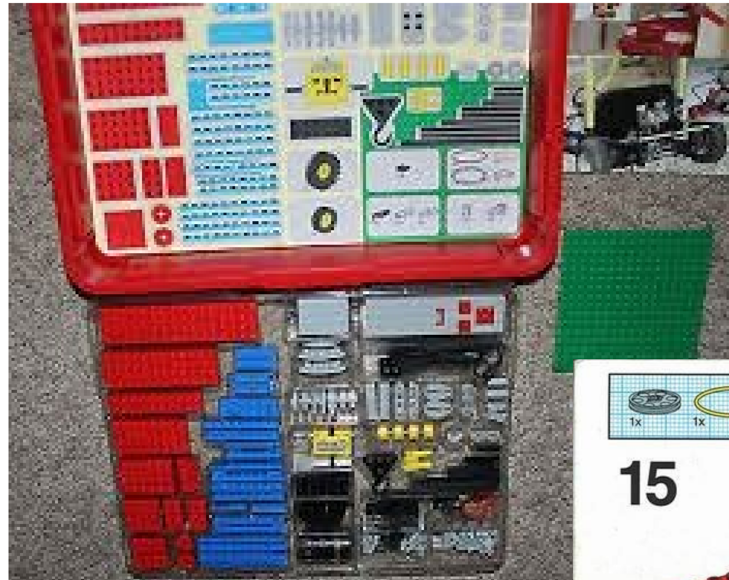
Revolutions in Physics - 1989

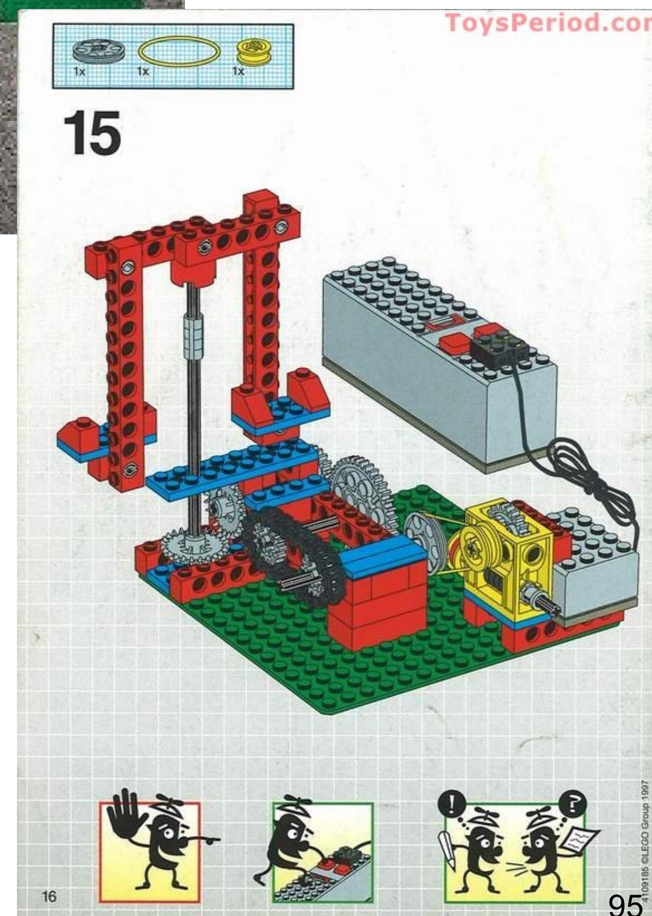
- Copernican astronomy
- Newtonian mechanics and causality
- The energy concept
- Entropy and probability
- Relativity
- Quantum theory and the end of causality
- Conservation principles and symmetries



Honors 185 a/b – Physics of Technology 1990-1995







- Lab – Disassemble, explain and reassemble a Briggs & Stratton four-cycle lawn mower engine; examine Volvo car parts; water hydraulics…
- Tour – Vanderbilt's steam plant; Air Force wind tunnel, Corvette plant, Peterbilt truck plant…
- Midterm – Build a Lego car powered by a mousetrap
- Final – Build a car with a four-speed transmission

JPW Learning Timeline

1949 Born to Leonora and John Wikswo, Sr.
1955-1967 Apprenticed to John Wikswo, Sr.

You can learn a lot by watching stuff done right. Doing it yourself might be better.

1965 Admitted early decision to the University of Virginia
1966 Started at UVa as an Echols Scholar (8 required courses)

Putting lots of smart students in single dorm is interesting.
Smart students can figure out what they need to learn.

1967-1970 Worked with Dr. Bascom Deaver and his graduate students

Having a skill is a foot in the door.
You learn by making, and by making mistakes.

1969-1970 Junior Fellow, UVa Society of Fellows

"How to give a mosquito an enema," Parti Québécois

Scholarly social environments can benefit learning.

1970-1975 Graduate School, Stanford

The Zen of Graduate Education: A PhD is a state of mind.

1975-1977 Postdoc, Stanford School of Medicine
1977- Joined the Vanderbilt faculty
1979 Co-founded the W.H. Sefam School

You learn quickly in a 24-7 immersion environment. Everyone learns differently.

1979 Co-sued Williamson County Superintendent of Schools and School Board

Learning without boxes scares some people.

1983 Proposed the College Scholars Program

Outstanding students need outstanding classes, not boxes to check.

1987 Taught one of the first College Scholars Seminars

Revolutions in Physics, How Things Work, What is Life? Origins of Life, The Microbiome

2006 Created the Searle Systems Biology and Bioengineering Undergraduate Research Experience (SyBBURE Searle)

Students benefit from being asked questions that have not yet been answered.

JPW Lessons Learned

- **You can learn a lot by watching stuff done right. Doing it yourself might be better.**
- **Putting lots of smart students in single dorm is interesting.**
- **Smart students can figure out what they need to learn.**
- **Having a skill is a foot in the door.**
- **You learn by making, and by making mistakes.**
- **Scholarly social environments can benefit learning.**
- **The Zen of Graduate Education: A PhD is a state of mind.**
- **You learn quickly in a 24-7 immersion environment. Everyone learns differently.**
- **Learning without boxes scares some people.**
- **Outstanding students need outstanding classes, not boxes to check.**
- **It's fun to be asked questions that have not yet been answered. <u>Especially if you are an undergraduate!</u>**

John Wikswo's CV

VIIBRE

Curriculum Vitae
JOHN PETER WIKSWO, JR.
October 2021

Vanderbilt Institute for Integrative Biosystems Research and Education
6301 Stevenson Center
Vanderbilt University
Nashville, TN USA 37235
Phone: (615) 343-4124 Fax: (615) 322-4977
Email: john.wikswo@vanderbilt.edu
http://www.vanderbilt.edu/viibre/Wikswo.html
ORCID: 0000-0003-2790-1530

FIELDS OF SPECIALIZATION: Biosystems science and engineering. Biological physics, systems biology, biomedical engineering, cellular instrumentation and control, microfabrication, organs-on-chips, automated biology, cardiac electrophysiology, electromagnetism, and SQUID magnetometry.

DEGREES:
B.A. - Physics, University of Virginia, Charlottesville, VA, 1970
M.S. - Physics, Stanford University, Stanford, CA, 1973
Ph.D. - Physics, Stanford University, Stanford, CA, 1975

APPOINTMENTS:

Research Fellow in Cardiology, Stanford University	1975-1977
Assistant Professor of Physics, Vanderbilt University	1977-1982
Associate Professor of Physics, Vanderbilt University	1982-1988
Professor of Physics, with tenure, Vanderbilt University	1988-present
A. B. Learned Professor of Living State Physics, Vanderbilt University	1991-2001
Gordon A. Cain University Professor, Vanderbilt University	2001-present
Professor of Biomedical Engineering, with tenure, Vanderbilt University	2001-present
Professor of Molecular Physiology and Biophysics, with tenure, Vanderbilt University School of Medicine	2001-present
Founding Director, Vanderbilt Institute for Integrative Biosystems Research and Education	2001-present
A. B. Learned Professor of Living State Physics, Vanderbilt University	2005-present
Member, Vanderbilt Ingram Cancer Center	2006-present
Visiting Member, Institute for Advanced Study, Princeton University	2007

HONORS:
Echols Scholar, University of Virginia, 1966-1970
Phi Beta Kappa, 1968
Junior Fellow, University of Virginia Society of Fellows, 1969-1970
B.A. with Highest Distinction, 1970
Woodrow Wilson Fellow, 1970
Woodrow Wilson Independent Study Award, 1970
NSF Predoctoral Fellow 1971-1974
Student Member, Institute for Electrical and Electronic Engineers, 1975
Member, Institute for Electrical and Electronic Engineers, 1975-2004
Bay Area Heart Research Committee Fellow, 1975-1977
Finalist, Deborah Heart and Lung Foundation Young Investigator Competition, 1980
Alfred P. Sloan Research Fellow, 1980-1982
IR-100 Award for Neuromagnetic Current Probe, 1984
Fellow, American Physical Society, 1990
John Simon Guggenheim Fellow, 1992-1993

1

HONORS (continued):
Thomas Jefferson Award, Vanderbilt University, 1997
Fellow, American Institute for Medical and Biological Engineering, 1999
Fellow of the American Heart Association, Fellow of the Council on Basic Cardiovascular Sciences of the American Heart Association, 2001
Fellow, Biomedical Engineering Society (BMES), 2005
Senior Member, Institute for Electrical and Electronic Engineers, 2005-2007
Fellow, Heart Rhythm Society, 2006
The Nightingale Prize 2006 for the best paper published in Medical and Biological Engineering and Computing in 2005
Fellow, Institute for Electrical and Electronic Engineers, 2008
Fellow, American Association for the Advancement of Science (AAAS), 2010
Full Member, Society of Toxicology (SOT), 2016
R&D 100 Award for MultiWell MicroFormulator, 2017
Experimental Biology and Medicine (EBM) Outstanding Reviewer Award, 2021

PROFESSIONAL SOCIETIES:
American Association for the Advancement of Science
American Heart Association
American Institute for Medical and Biological Engineering
American Physical Society: Division of Biological Physics, Division of Material Physics; Instrument and Measurement Science Topical Group
American Physiological Society
Biomedical Engineering Society (BMES)
Biophysical Society
Heart Rhythm Society
Institute for Electrical and Electronic Engineers: Engineering in Medicine and Biology Society; Magnetics Society (S'75–M'75–SM'05–F'08)
Sigma Xi (– 2020)
Society for Mathematical Biology
Society of Toxicology
Tennessee Academy of Science
Union of Concerned Scientists

EXTERNAL ACTIVITIES:

Technician, Department of Physics, University of Virginia, 1967-1970
Vice-President, Dexmach, Inc., Palo Alto, CA, 1975-1977
Consultant, David W. Taylor Naval Ship Research and Development Center, Annapolis, MD, 1976-1982
Consultant, Cardiology Division, Stanford University School of Medicine, 1977-1983
Consultant, Cardiac Pacemakers, Inc., Minneapolis, MN, 1985-1988
Director of Undergraduate Studies, Department of Physics and Astronomy, Vanderbilt University, 1985-1989
Advisory Board, National Vibrating Probe Facility, Marine Biological Laboratory, Woods Hole, MA 1986-88
Program Committee (North and South America), Sixth World Conference on Biomagnetism, Tokyo, 1987
International Advisory Committee on Biomagnetism, 1987-1993
Scientific Advisory Board, Hypres, Inc., 1989-present (currently inactive)
Consultant, Marion Merrell Dow, Inc., 1990-1991
Nominating Committee, Division of Biological Physics, American Physical Society, 1991-1992
Executive Board, Learning Community Design Team, Vanderbilt University, 1992-1993
Consultant, Capital Case Resource Center, Nashville, TN, 1992-1994
Consultant, E.I. du Pont de Nemours & Company, 1989-1993
Advisory Board, The Jasper Project, Peabody College for Teachers, Vanderbilt University, 1990-1996

2

https://www.vanderbilt.edu/viibre/documents/WikswoCV.pdf

John Wikswo's CV, pages 27-28

PUBLICATIONS (continued):

214. "Methods To Identify Saline-Contaminated Electrolyte Profiles," D. Patel, R. Naik, R. Boyer, J. Wikswo, E. Vasilevskis, Clin. Chem. Lab. Med., 53(10): 1585-1591 (2015). DOI: 10.1515/cclm-2014-0955. PMCID: PMC4544643
215. "Structuring Microbial Metabolic Responses to Multiplexed Stimuli Via Self-Organizing Metabolomics Maps," C.R. Goodwin, B.C. Covington, D.K. Derewacz, C.R. McNees, J.P. Wikswo, J.A. McLean, B.O. Bachmann, Chem. Biol., 22: 661-670 (2015). DOI: 10.1016/j.chembiol.2015.03.020. PMCID: PMC4537791
216. "Glutamine and Glutamate Limit the Shortening of Action Potential Duration in Anoxia-Challenged Rabbit Hearts," K.J. Drake, M.S. Shotwell, J.P. Wikswo, and V.Y. Sidorov, Phys. Rep., 3(9): e12535 (2015). DOI: 10.14814/phy2.12535, PMCID: PMC4600381
217. "Recreating Blood-Brain Barrier Physiology and Structure On Chip: A Novel Neurovascular Microfluidic Bioreactor," J.A. Brown, V. Pensabene, D. A. Markov, V. Allwardt, D.M. Neely, M. Shi, C.M. Britt, O.S. Hoilett, Q. Yang, B.M. Brewer, P.C. Samson, L.J. McCawley, J.M. May, D.J. Webb, D. Li, A.B. Bowman, R.S. Reiserer, and J.P. Wikswo, Biomicrofluidics, 9:054124 (2015). DOI: 10.1063/1.4934713. PMCID: PMC4627929
218. "Real-Time Monitoring of Cellular Bioenergetics with a Multianalyte Screen-Printed Electrode," J.R. McKenzie, A.C. Cognata, A.N. Davis, J.P. Wikswo, and D.E. Cliffel, Anal. Chem., 87:7857-7864 (2015). DOI: 10.1021/acs.analchem.5b01533. PMCID: PMC4770793
219. "Development of Novel Murine Mammary Imaging Windows to Examine Leukocyte Trafficking and Metastasis of Mammary Tumors with Intravital Imaging," T. Sobolik, Y. Su, W. Ashby, D.K. Schaffer, S. Wells, J.P. Wikswo, A. Zijlstra, and A. Richmond, IntraVital, 5:e1125562 (2016). DOI: 10.1080/21659087.2015.1125562, PMCID: PMC5226013
220. "Ultrathin Polymer Membranes with Patterned, Micrometric Pores for Organs-on-Chips," V. Pensabene, L. Costa, A.Y. Terekhov, J.S. Gnecco, J.P .Wikswo, W.H. Hofmeister, ACS Appl. Mater. Interfaces, 8:22629-22636 (2016) DOI: 10.1021/acsami.6b05754. PMCID: PMC5131702
221. "Metabolic Consequences of Inflammatory Disruption of the Blood-Brain Barrier in an Organ-on-Chip Model of the Human Neurovascular Unit," J.A. Brown, S.G. Codreanu, M. Shi, S.D. Sherrod, D.A. Markov, M.D. Neely, C.M. Britt, O.S. Hoilett, R.S. Reiserer, P.C. Samson, L.J. McCawley, D.J. Webb, A.B. Bowman, J.A. McLean, J.P. Wikswo, J. Neuroinflammation, 13:306 (2016) DOI: 10.1186/s12974-016-0760-y. PMCID: PMC5153753
222. "I-Wire Heart-on-a-Chip I: Three-Dimensional Cardiac Tissue Constructs for Physiology and Pharmacology," V.Y. Sidorov, P.C. Samson, T.N. Sidorova, J.M. Davidson, C.C. Lim, J.P. Wikswo, Acta Biomater., 48:68-78 (2017) DOI: 10.1016/j.actbio.2016.11.009. PMCID: PMC5235983
223. "I-Wire Heart-on-a-Chip II: Biomechanical Analysis of Contractile, Three-Dimensional Cardiomyocyte Tissue Constructs," A.K. Schroer, M.S. Shotwell, V.Y. Sidorov, J.P. Wikswo, W.D. Merryman, Acta Biomater., 48:79-87 (2017) DOI: 10.1016/j.actbio.2016.11.010. PMCID: PMC5235976
224. "Functional Coupling of Human Microphysiology Systems: Intestine, Liver, Kidney Proximal Tubule, Blood-Brain Barrier and Skeletal Muscle," L. Vernetti, A. Gough, N. Baetz, S. Blutt, J.R. Broughman, J.A. Brown, J. Foulke-Abel, N. Hasan, J. In, E. Kelly, O. Kovbasnjuk, J. Repper, N. Senutovitch, J. Stabb, C. Yeung, N.C. Zachos, M. Donowitz, M. Estes, J. Himmelfarb, G. Truskey, J. Wikswo, D.L. Taylor, Sci. Rep., 7:42296 (2017) DOI: 10.1038/srep42296. PMCID: PMC5296733

27

PUBLICATIONS (continued):

225. "Integrated, High-Throughput, Multi-Omics Platform Enables Data-Driven Construction of Cellular Responses and Reveals Global Drug Mechanisms of Action," J.L. Norris, M.A. Farrow, D.B. Gutierrez, L.D. Palmer, N. Muszynski, S.D. Sherrod, J.C. Pino, J.L. Allen, J.M. Spraggins, A.L.R. Lubbock, A. Jordan, W. Burns, J.C. Poland, C. Romer, M.L. Manier, Y. Nei, B.M. Prentice, K.L. Rose, S. Hill, R. Van de Plas, T. Tsui, N.M. Braman, M.R. Keller, S.A. Rutherford, N. Lobdell, C.F. Lopez, D.B. Lacy, J.A. McLean, J.P. Wikswo, E.P. Skaar, R.M. Caprioli, J. Proteome Res., 16:1364-1375 (2017) DOI: 10.1021/acs.jproteome.6b01004
226. "Circadian Hormone Control in a Human-on-a-Chip: *In Vitro* Biology's Ignored Component?," K.J. Cyr, O.M. Avaldi, J.P. Wikswo, Exp. Biol. Med., 242:1714-1731 (2017) DOI: 10.1177/1535370217732766, PMCID: PMC5832251
227. "Engineered Microfluidic Bioreactor for Examining the Three-Dimensional Breast Tumor Microenvironment," M. Rogers, T. Sobolik, D.K. Schaffer, P.C. Samson, A. Johnson, P. Owens, S.G. Codreanu, S.D. Sherrod, J.A. McLean, J.P. Wikswo, A. Richmond, Biomicrofluidics, 12:034102 (2018), DOI: 10.1063/1.5016433, PMCID: PMC5938175
228. "A Simplified, Fully Defined Differentiation Scheme for Producing Blood-Brain Barrier Endothelial Cells from iPSCs," E.H. Neal, N.A. Marinelli, Y. Shi, P.M. McClatchey, K.M. Balotin, D.R. Gullett, K.A. Hagerla, A.B. Bowman, K.C. Ess, J.P. Wikswo, E.S. Lippmann, Stem Cell Reports, 12:1380-1388 (2019) DOI: 10.1016/j.stemcr.2019.05.008, PMCID: PMC6565873
229. "The Microbiome and the Gut-Liver-Brain Axis for CNS Clinical Pharmacology: Challenges in Specifying and Integrating In Vitro and In Silico Models," K.G. Hawkins, C. Casolaro, J.A. Brown, D.A. Edwards, J.P. Wikswo, Clinical Pharmacology and Therapeutics, 108:929-948 (2020) DOI: 10.1002/cpt.1870, PMCID: PMC7572575 (State of the Art article)
230. "Advances in Blood-Brain Barrier Modeling in Microphysiological Systems Highlight Critical Differences in Opioid Transport Due to Cortisol Exposure," J. Brown, S. Faley, Y. Shi, K. Hillgren, G. Sawada, T. Baker, J. Wikswo, E. Lippmann, Fluids and Barriers of the CNS, 17:38 (2020) DOI: 10.1186/s12987-020-00200-9, PMCID: PMC7269003
231. "Predicting Susceptibility to SARS-CoV-2 Infection Based on Structural Differences in ACE2 Across Species," M.R. Alexander, C.T. Schoeder, J.A. Brown, C.D. Smart, C. Moth, J.P. Wikswo, J.A. Capra, J. Meiler, W. Chen, M.S. Madhur, FASEB Journal, 34:15946-15960 (2020) doi: 10.1096/fj.202001808R, PMCID: PMC7675292
232. "A bistable, multiport valve enables microformulators creating microclinical analyzers that reveal aberrant glutamate metabolism in astrocytes derived from a tuberous sclerosis patient," D.R. Miller, D.K. Schaffer, M.D. Neely, E.S. McLain, A.R Travis, F.E. Block III, J. McKenzie, E.M. Werner, L. Armstrong, D.A. Markov, A.B. Bowman, K.C. Ess, D.E. Cliffel, J.P. Wikswo, Sensors and Actuators B: Chemical, 341: 129972 (2021) doi: 10.1016/j.snb.2021.129972, PMCID: PMC8174775

Book Chapters

1. "Theory and Application of Magnetocardiography," J.P. Wikswo, Jr., J.A.V. Malmivuo, W.H. Barry, M.C. Leifer, and W.M. Fairbank, in Cardiovascular Physics, D.N. Ghista, E. Van Vollenhoven, and W. Yang, Eds., (Karger, Basil) pp. 1-67 (1979).
2. "Cellular Action Currents," J.P. Wikswo, Jr., in Biomagnetism: An Interdisciplinary Approach, S.J. Williamson, G.-L. Romani, L. Kaufman, and I. Modena, Eds., (Plenum, New York), pp. 173-207 (1983).
3. "Theoretical Aspects of the ECG-MCG Relationship," J.P. Wikswo, Jr., in Biomagnetism: An Interdisciplinary Approach, S.J. Williamson, G.-L. Romani, L. Kaufman, and I. Modena, Eds., (Plenum, New York), pp. 311-326 (1983).

No matter the size of your CV, there will always be someone with a longer CV.

28

https://www.vanderbilt.edu/viibre/documents/WikswoCV.pdf

2019

VI∫BRE

ac action activity advanced afosr aging air aircraft alan allos aluminum analysis analytical anisotropic anisotropy apparatus applied approach array arrhythmias aspects assays assessment automated axon barrier bidomain bioelectric bioengineering biological biology biomagnetism biomedical biomems biophysics bioreactors blood-brain bme bowel bruno building bundles calculation cancer cardiac cardiology cardiovascular care cell cellular challenges chambers changes characterization chemical chemistry chemotaxis chip circle clinical closing comparison complex compound computer conduction conductor constructs control corporation corrosion course cryocoolers currents darpa data dc defects defense defibrillation delivery design detection determination development device discovery disease distributions division drug dynamics early eeg effects eklund electrical electrode electromagnetic electronic electrophysiology element embs environment evaluation experiment experimental extension fabrication fibers field finite flaws flow fluidic food force forward foundation function fund fundamental future gastrointestinal general gielen heart hidden high-resolution human hypres imaging implications improved individual inference information initiative injection innovations instrumentation integrated interactions intestinal inverse investigation ischemia ischemic isolated issue kotani lead leboeuf life liu magnetic magnetocardiography magnetometer magnetometry mapping mashburn mass materials mathematical max measurements mechanisms medical medicine metabolic method micro microdevices microfabricated microfluidic microphysiological microscope microscopy migration models molecular monitoring multi-omics multiple muscle myocardial nasa nato ncats nci nde nerve network neuroscience neurovascular nih non-destructive non-invasive nondestructive novel nsf ny oh opportunities optical organ-on-a-chip organ-on-chip organs organs-on-chips parallel perfused peripheral perspectives pharmacology phase physics physiology planar planning platform plenum possible potential power predictive present probe problems progress propagation publishers pumps qnde quantitative quantum rabbit rapid rate real-time recent reentry resolution response roden rotary safety scaling search sensing sensitivity sensors shotwell signaling simulation single skeletal small smith sources space spatial spectrometry spie squid states status stimulation structure study superconducting susceptibility systems technical techniques technology testing theoretical theory threat three-dimensional tissue tomography tools towards toxicity toxicology toxins translational two-dimensional usaf va valves vector view virtual vitro vivo volume working yang

John Wikswo

Gordon Cain University Professor; Founding Director of VIIBRE

Organs-on-a-Chip
Cellular Instrumentation and Control
Automated Biology
Tissue Chips

	All	Since 2016
Citations	15831	4843
h-index	63	37
i10-index	285	117

3 articles — 77 articles

not available — available

Based on funding mandates

TITLE	CITED BY	YEAR
Using a magnetometer to image a two-dimensional current distribution BJ Roth, NG Sepulveda, JP Wikswo Jr Journal of applied physics 65 (1), 361-372	497	1989
Virtual electrodes in cardiac tissue: a common mechanism for anodal and cathodal stimulation JP Wikswo Jr, SF Lin, RA Abbas Biophysical journal 69 (6), 2195-2210	418	1995
Current injection into a two-dimensional anisotropic bidomain NG Sepulveda, BJ Roth, JP Wikswo Jr Biophysical journal 55 (5), 987-999	414	1989
Effects of flow and diffusion on chemotaxis studies in a microfabricated gradient generator GM Walker, J Sai, A Richmond, M Stremler, CY Chung, JP Wikswo Lab on a Chip 5 (6), 611-618	309	2005
Recreating blood-brain barrier physiology and structure on chip: A novel neurovascular microfluidic bioreactor JA Brown, V Pensabene, DA Markov, V Allwardt, MD Neely, M Shi, ... Biomicrofluidics 9 (5), 054124	283	2015
SQUID magnetometers for biomagnetism and nondestructive testing: important questions and initial answers JP Wikswo IEEE Transactions on Applied Superconductivity 5 (2), 74-120	260	1995
Scaling and systems biology for integrating multiple organs-on-a-chip JP Wikswo, EL Curtis, ZE Eagleton, BC Evans, A Kole, LH Hofmeister, ... Lab on a Chip 13 (18), 3496-3511	255	2013
Microfluidic single-cell array cytometry for the analysis of tumor apoptosis D Wlodkowic, S Faley, M Zagnoni, JP Wikswo, JM Cooper Analytical chemistry 81 (13), 5517-5523	238	2009
SQUIDs for nondestructive evaluation WG Jenks, SSH Sadeghi, JP Wikswo Jr Journal of Physics D: Applied Physics 30 (3), 293	238	1997
Magnetic field of a nerve impulse: first measurements JP Wikswo, JP Barach, JA Freeman Science 208 (4439), 53-55	238	1980
Reduction of infarct size with the early use of timolol in acute myocardial infarction International Collaborative Study Group New England Journal of Medicine 310 (1), 9-15	237	1984
A low temperature transfer of ALH84001 from Mars to Earth BP Weiss, JL Kirschvink, FJ Baudenbacher, H Vali, NT Peters, ... Science 290 (5492), 791-795	233	2000
Scanning SQUID microscopy JR Kirtley, JP Wikswo Jr Annual Review of Materials Science 29 (1), 117-148	187	1999
The relevance and potential roles of microphysiological systems in biology and medicine JP Wikswo Experimental biology and medicine 239 (9), 1061-1072	171	2014
Functional coupling of human microphysiology systems: intestine, liver, kidney proximal tubule, blood-brain barrier and skeletal muscle L Vernetti, A Gough, N Baetz, S Blutt, JR Broughman, JA Brown, ... Scientific reports 7 (1), 1-15	162	2017

VIIBRE

Google

john wikswo

All | News | Images | Maps

About 42,100 results (0.53 seconds)

John Wikswo

Physicist

John Wikswo

Gordon Cain University Professor; Founding Director of VIIBRE

Organs-on-a-Chip
Cellular Instrumentation and Control
Automated Biology
Tissue Chips

	All	Since 2016
Citations	15831	4843
h-index	63	37
i10-index	285	117

3 articles — not available
77 articles — available

albert-lászló barabási

All · News · Images · Videos · Shopping · More · Tools

About 217,000 results (0.59 seconds)

Albert-László Barabási (Barabási Albert Lász...
American-Hungarian-Romanian physicist

No matter the size of your *h factor*, there will always be someone with a bigger *h factor*.

Albert-László Barabási

FOLLOW

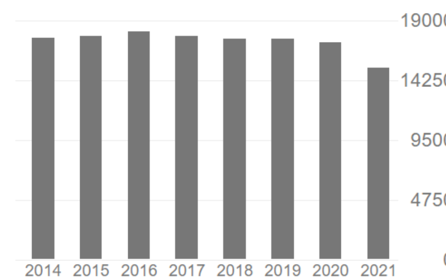
Northeastern University, Harvard Medical School
Verified email at neu.edu - Homepage

network science · statistical physics · biological physics · physics · medicine

TITLE	CITED BY	YEAR
Emergence of scaling in random networks AL Barabási, R Albert Science 286 (5439), 509-512	40519	1999
Statistical mechanics of complex networks R Albert, AL Barabasi Reviews of Modern Physics 74, 47-97	24815	2002
Authoritative sources in a hyperlinked environment JM Kleinberg, M Newman, AL Barabási, DJ Watts The structure and dynamics of networks, 514-542	10971	2011
Linked: The New Science Of Networks AL Barabási Basic Books	10540 *	2002

Cited by — VIEW ALL

	All	Since 2016
Citations	272992	103354
h-index	160	120
i10-index	375	296

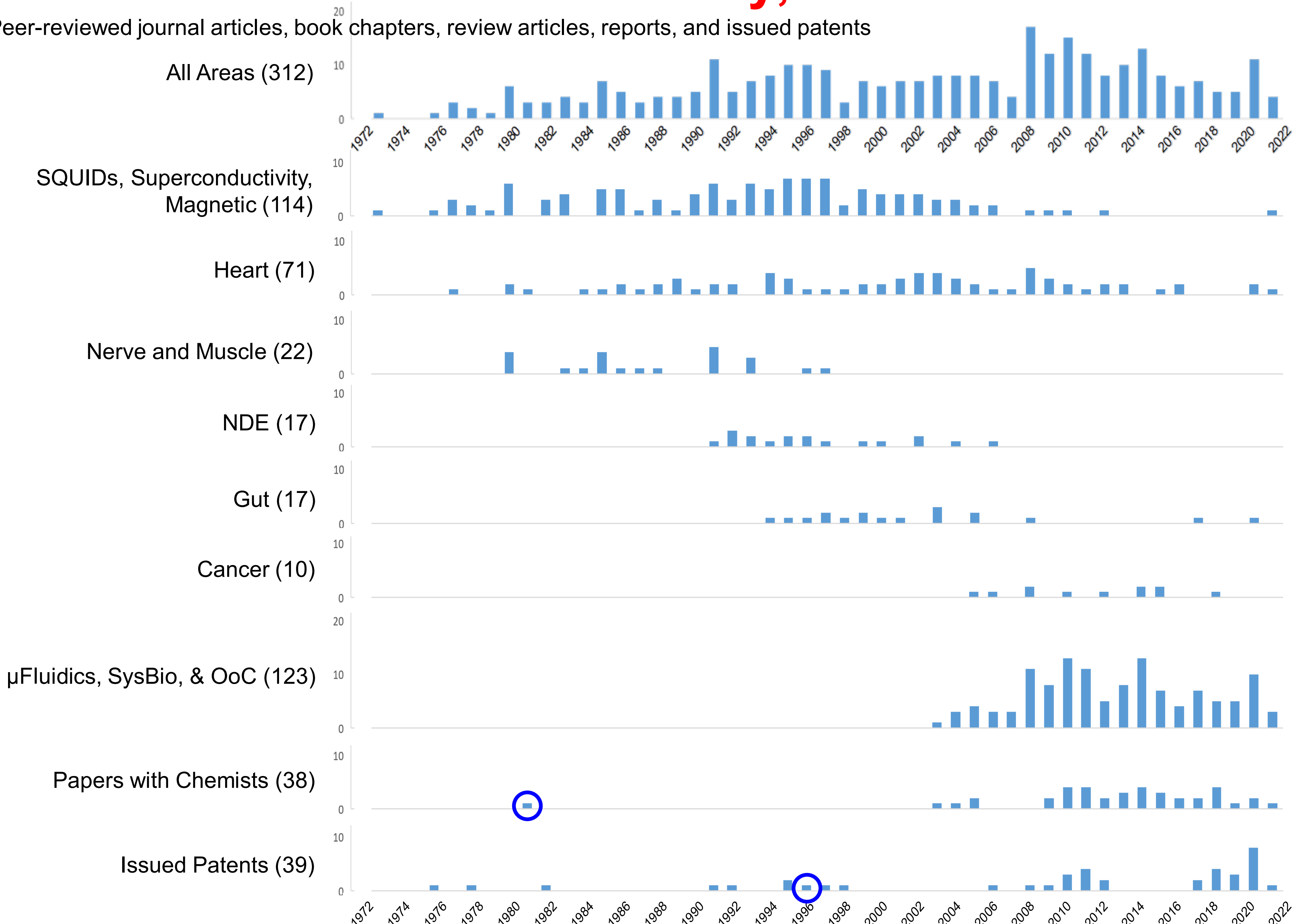


Public access — VIEW ALL

3 articles — 93 articles

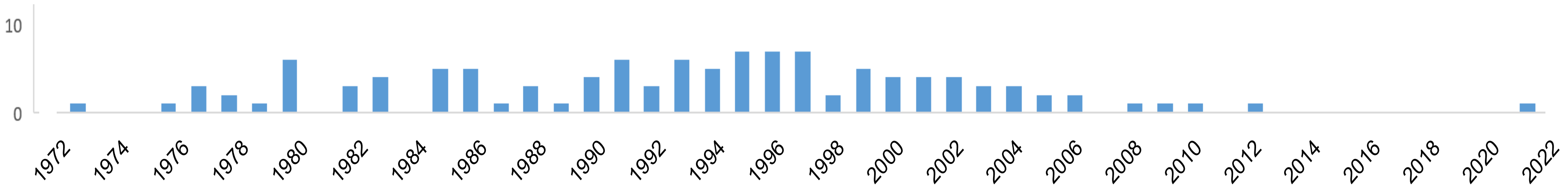
John Wikswo Research Activity, 1966-2021

Peer-reviewed journal articles, book chapters, review articles, reports, and issued patents



SQUIDs, Superconductivity, Magnetism (114)

- 1967 to ~2010
- 114 peer-reviewed journal articles, book chapters, review articles, reports, and issued patents



- I built LOTS of cryogenic instruments as a technician at the University of Virginia.
- My junior project measured the superfluid helium lambda transition.
- When I left UVa, my senior project on the AC Josephson Effect morphed into another graduate student's PhD dissertation.
- I continued my work with SQUID magnetometers for 40 years.

John Wikswo

Gordon Cain University Professor; Founding Director of VIIBRE

Organs-on-a-Chip
Cellular Instrumentation and Control
Automated Biology
Tissue Chips

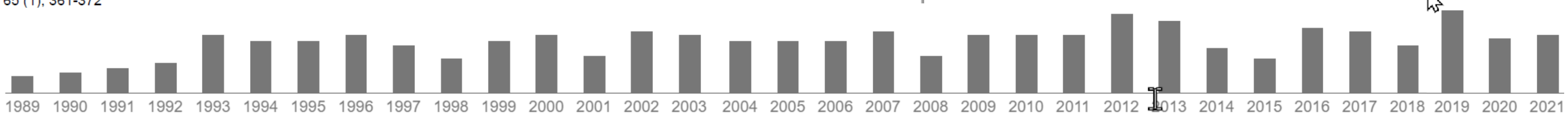
	All	Since 2016
Citations	15831	4843
h-index	63	37
i10-index	285	117

3 articles — 77 articles

not available — available

Based on funding mandates

TITLE	CITED BY	YEAR
Using a magnetometer to image a two-dimensional current distribution BJ Roth, NG Sepulveda, JP Wikswo Jr Journal of applied physics 65 (1), 361-372	497	1989



Using a magnetometer to image a two-dimensional current distribution

Bradley J. Roth,[a] Nestor G. Sepulveda, and John P. Wikswo, Jr.
Living State Physics Group and Vanderbilt Electromagnetics Laboratory, Department of Physics and Astronomy, Vanderbilt University, Nashville, Tennessee 37235

(Received 16 June 1988; accepted for publication 13 September 1988)

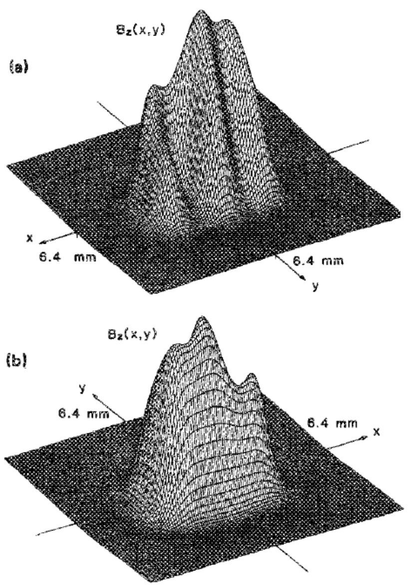


FIG. 1. Two views of simulated magnetometer data. The magnetometer coil, radius 0.35 mm, detected the normal component of the magnetic field, B_z, over a plane 1 mm above a two-dimensional current source. The magnetometer signal has an amplitude of 190 pT and contains 0.5 pT of noise. Our goal is to reconstruct an image of the current distribution that produced this magnetic field.

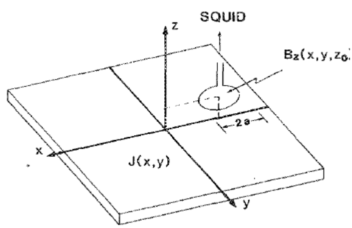


FIG. 2. Schematic diagram of the simulated experiment.

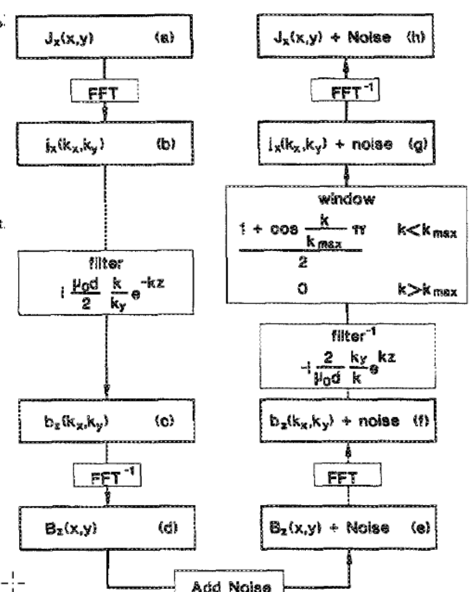


FIG. 4. Schematic diagram summarizing the forward and inverse problems. Starting with a known x component of the current density, $J_x(x,y)$, we calculate the z component of the magnetic field, $B_z(x,y,z)$, then add noise, and calculate an image of the current density from the noisy magnetic field.

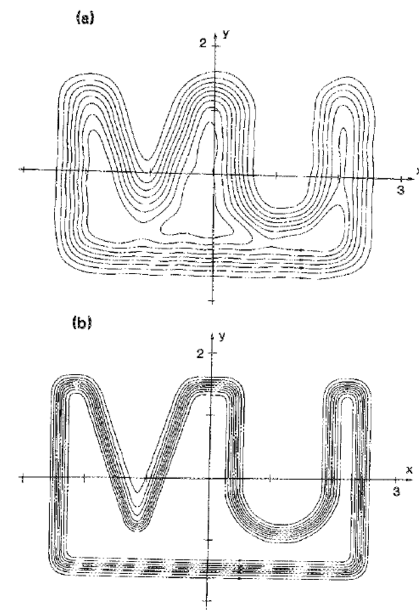
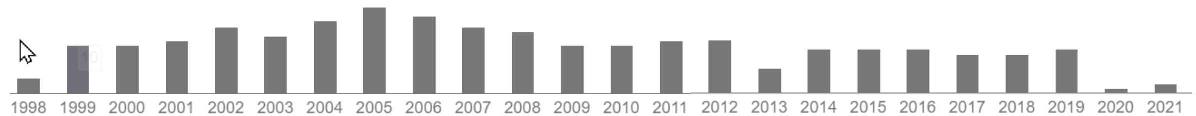


FIG. 12. (a) Image of the current density, calculated from the noisy magnetic field in Fig. 1: $z = 1.0$ mm, $k_{max} = 10$ mm^{-1}, noise = 0.5 pT, $a = 0.35$ mm, and MSD = 0.40. (b) Current density used to calculate the magnetic field in Fig. 1. The loop carries 1 μA of current, and the current profile across the loop cross section is Gaussian, with $\lambda = 0.15$ mm.

SQUIDs for nondestructive evaluation 238 1997

WG Jenks, SSH Sadeghi, JP Wikswo Jr

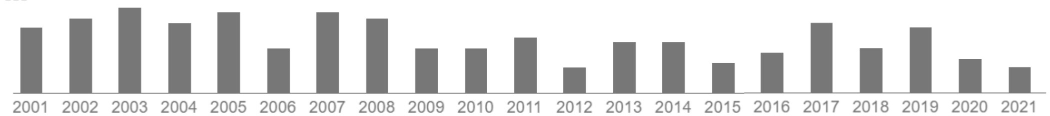
Journal of Physics D: Applied Physics 30 (3), 293



A low temperature transfer of ALH84001 from Mars to Earth 233 2000

BP Weiss, JL Kirschvink, FJ Baudenbacher, H Vali, NT Peters, ...

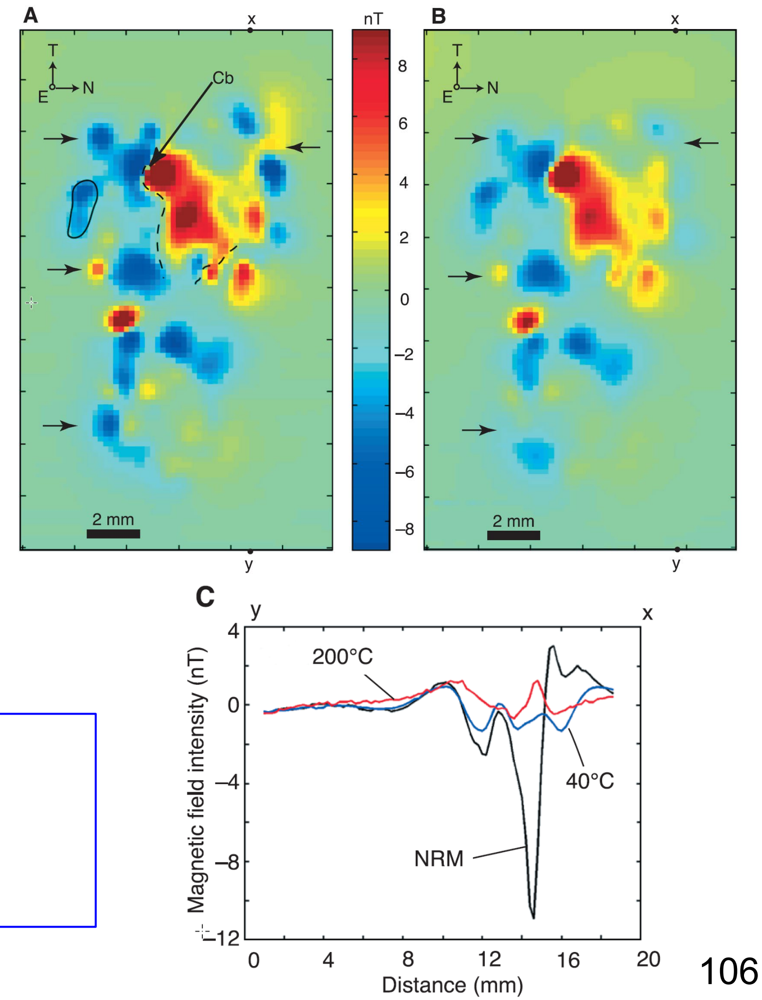
Science 290 (5492), 791-795



A Low Temperature Transfer of ALH84001 from Mars to Earth

Benjamin P. Weiss,[1]* Joseph L. Kirschvink,[1] Franz J. Baudenbacher,[2] Hojatollah Vali,[3] Nick T. Peters,[2] Francis A. Macdonald,[1] John P. Wikswo[2]

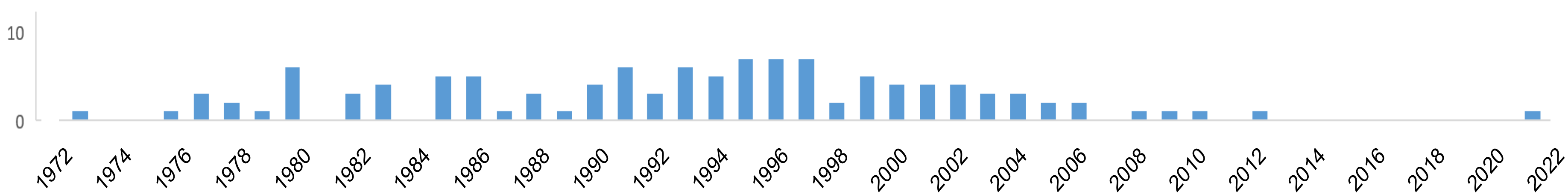
The ejection of material from Mars is thought to be caused by large impacts that would heat much of the ejecta to high temperatures. Images of the magnetic field of martian meteorite ALH84001 reveal a spatially heterogeneous pattern of magnetization associated with fractures and rock fragments. Heating the meteorite to 40°C reduces the intensity of some magnetic features, indicating that the interior of the rock has not been above this temperature since before its ejection from the surface of Mars. Because this temperature cannot sterilize most bacteria or eukarya, these data support the hypothesis that meteorites could transfer life between planets in the solar system.



These data were the first to support the hypothesis that meteorites could transfer life between the planets in the solar system.

SQUIDs, Superconductivity, Magnetism (114)

- 1967 to ~2010
- 114 peer-reviewed journal articles, book chapters, review articles, reports, and issued patents



I left the field because of the complexity and cost of the technology, the limits on the information delivered by magnetic measurements as compared to other techniques, and a difficult collaborator.

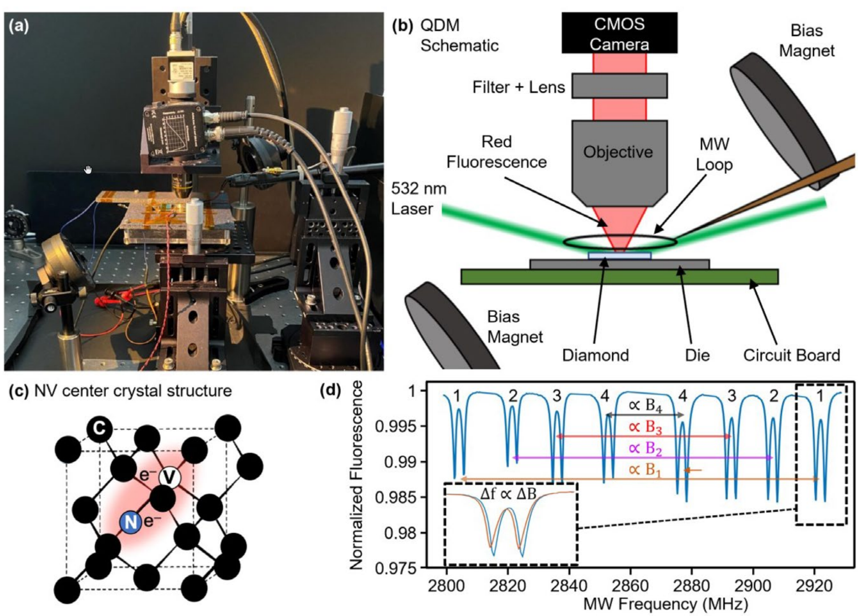
ISTFA 2021: Proceedings from the 47th International Symposium for
Testing and Failure Analysis Conference
October 31— November 4, 2021
Phoenix Convention Center, Phoenix, Arizona, USA
DOI: 10.31399/asm.cp.istfa2021p0096

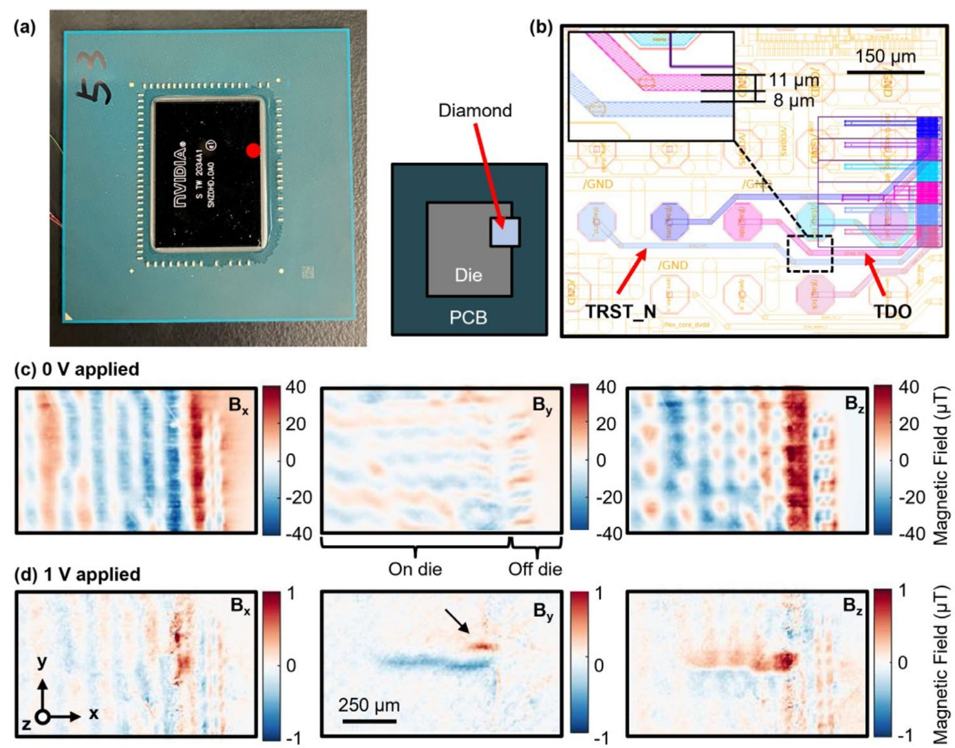
Vector Magnetic Current Imaging of an 8 nm Process Node Chip and 3D Current Distributions Using the Quantum Diamond Microscope

Sean M. Oliver,[1,2,*] Dmitro J. Martynowych,[1,*] Matthew J. Turner,[2,3,4] , David A. Hopper,[1] Ronald L. Walsworth,[2,3,4] and Edlyn V. Levine[1,2,5,§]

[1]The MITRE Corporation, McLean, VA 22102, United States of America
[2]Quantum Technology Center, University of Maryland, College Park, Maryland 20742, United States of America
[3]Department of Electrical and Computer Engineering, University of Maryland, College Park, Maryland, 20742, United States of America
[4]Department of Physics, University of Maryland, College Park, Maryland, 20742, United States of America
[5]Department of Physics, Harvard University, Cambridge, MA 02138, United States of America
**These authors contributed equally to this work*
[§]Corresponding author: evlevine@mitre-engenuity.org

This is a FANTASTIC development that uses our algorithm!

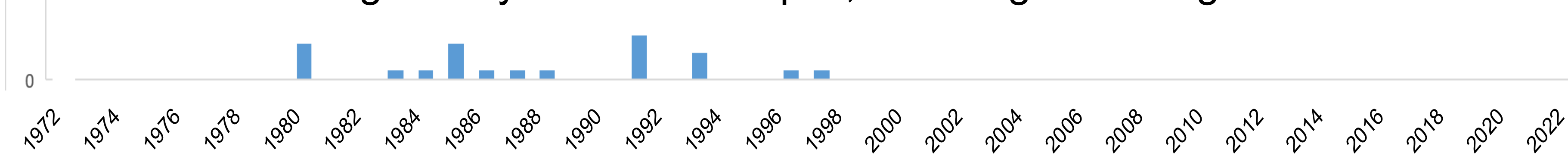




Nerve Axons and Skeletal Muscle

- 1977 to the present
- 22 peer-reviewed journal articles, book chapters, review articles, reports, and issued patents

Frog to crayfish to rat to squid, including modelling ...



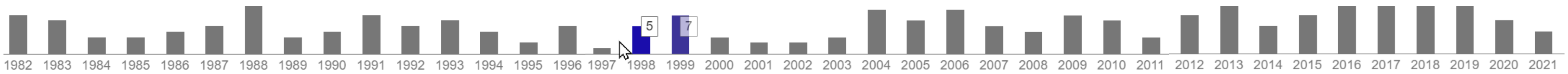
- I came to Vanderbilt in 1977 to make the first measurement of the magnetic field of a nerve.

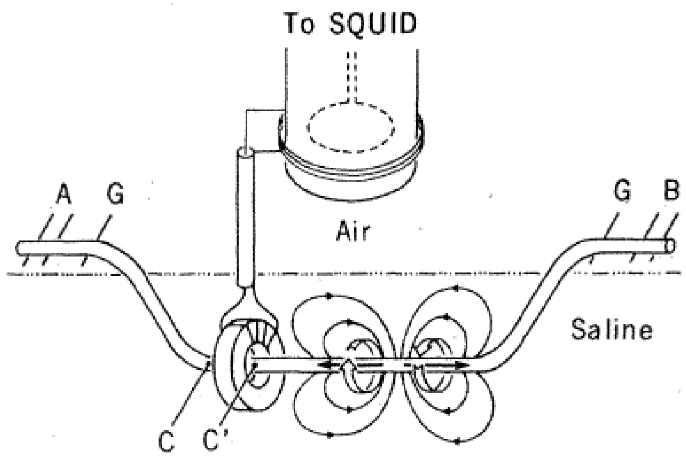
Magnetic field of a nerve impulse: first measurements

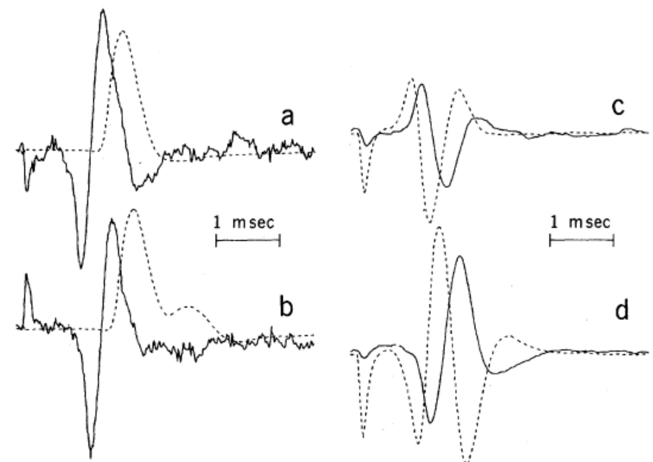
238 1980

JP Wikswo, JP Barach, JA Freeman

Science 208 (4439), 53-55





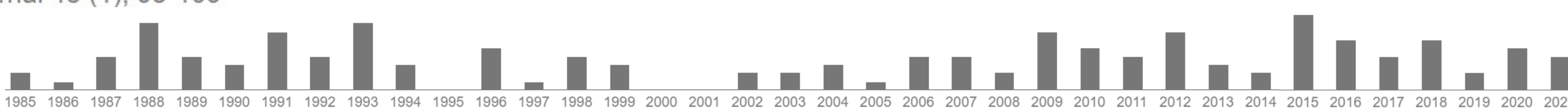


The magnetic field of a single axon. A comparison of theory and experiment

143 1985

BJ Roth, JP Wikswo Jr

Biophysical journal 48 (1), 93-109



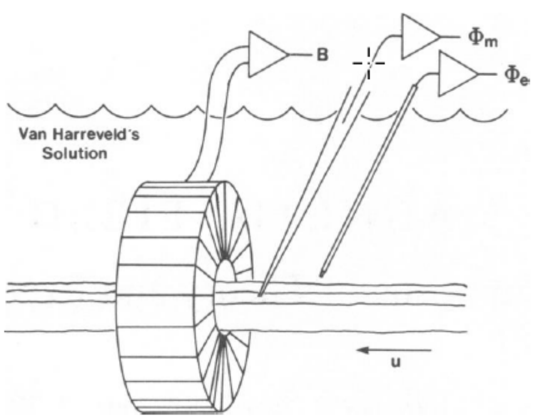
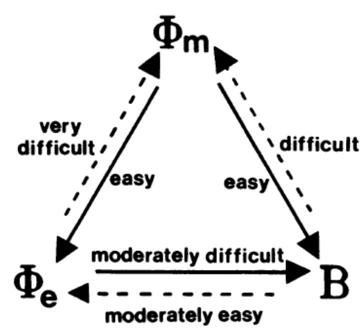
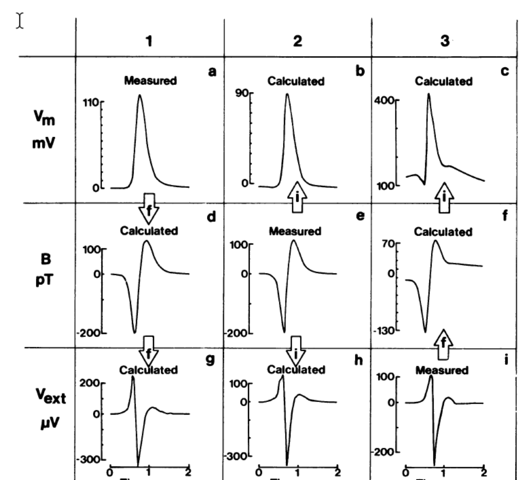


FIGURE 1 Schematic diagram of the experiment.

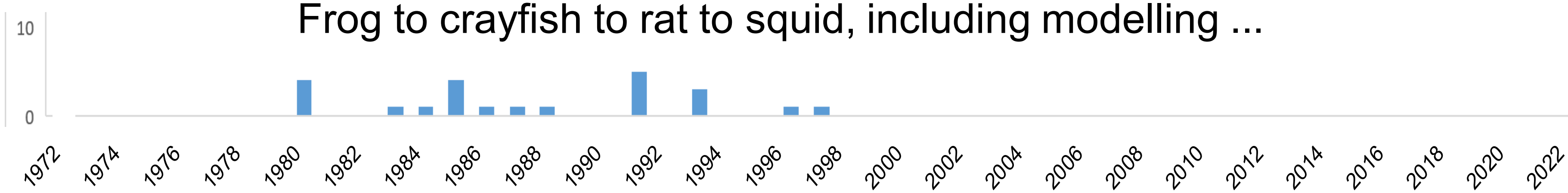




Nerve Axons and Skeletal Muscle

- 1977 to the present
- 22 peer-reviewed journal articles, book chapters, review articles, reports, and issued patents

Frog to crayfish to rat to squid, including modelling ...

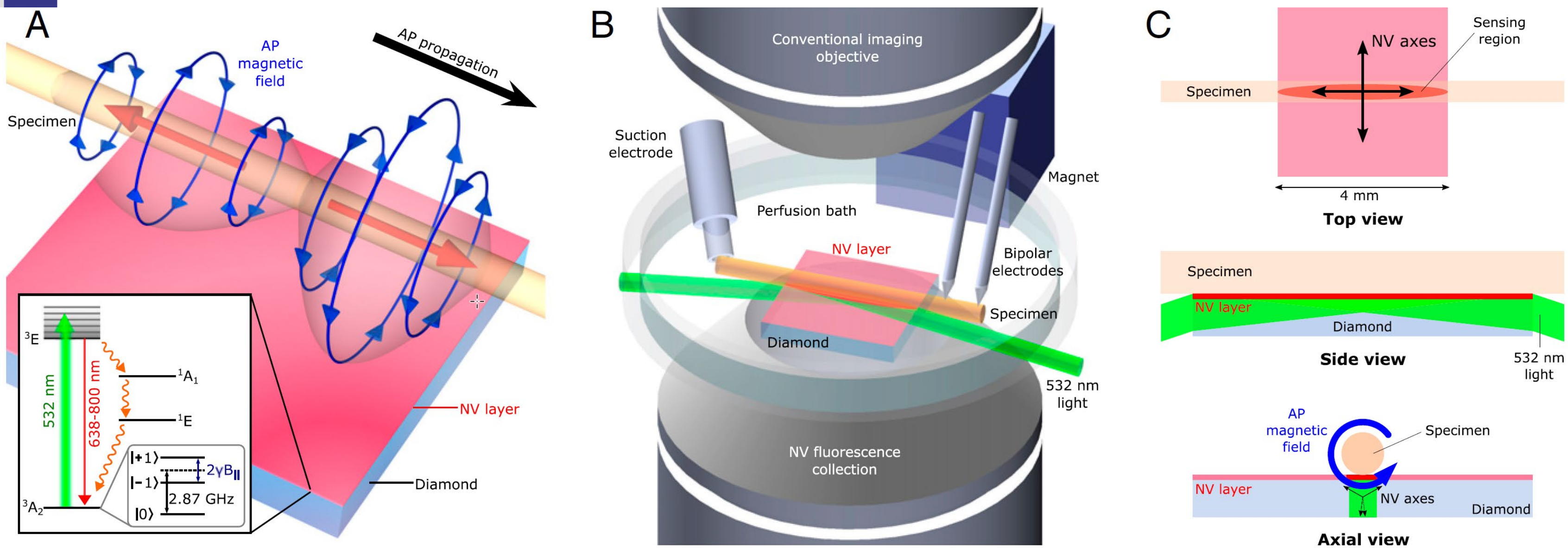


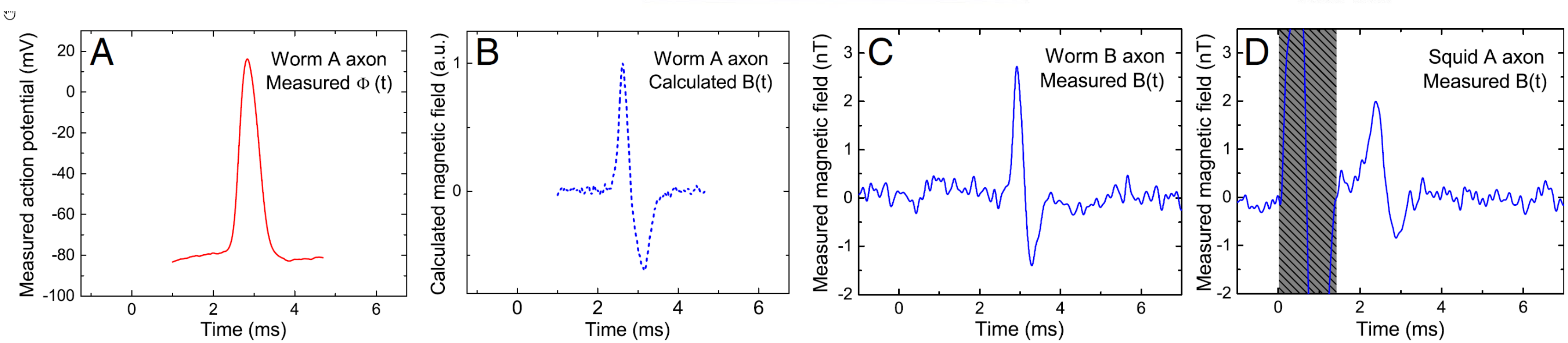
- I left the field in 1988 because of the power of patch clamp, the lack of clinical collaborators at VU, and my former PhD student Jan van Egeraat's untimely death from cancer. (He had a faculty position in the Netherlands and had started a company to make interoperative neuromagnetic measurements.)
- I might reenter the field with a colleague at Tulane who is developing a peripheral nerve on a chip and needs an easy way to measure conduction velocity.

Optical magnetic detection of single-neuron action potentials using quantum defects in diamond

John F. Barry[a,b,c], Matthew J. Turner[b,c], Jennifer M. Schloss[c,d], David R. Glenn[a,b,c], Yuyu Song[e,f,g,h], Mikhail D. Lukin[b], Hongkun Park[b,c,i,j], and Ronald L. Walsworth[a,b,c,1]

[a]Harvard-Smithsonian Center for Astrophysics, Cambridge, MA 02138; [b]Department of Physics, Harvard University, Cambridge, MA 02138; [c]Center for Brain Science, Harvard University, Cambridge, MA 02138; [d]Department of Physics, Massachusetts Institute of Technology, Cambridge, MA 02139; [e]Marine Biological Laboratory, Woods Hole, MA 02543; [f]Department of Genetics, Yale School of Medicine, New Haven, CT 06510; [g]Howard Hughes Medical Institute, Yale School of Medicine, New Haven, CT 06510; [h]Harvard Program in Therapeutic Science, Department of Systems Biology, Harvard Medical School, Boston, MA 02115; [i]Department of Chemistry and Chemical Biology, Harvard University, Cambridge, MA 02138; and [j]Broad Institute of MIT and Harvard, Cambridge, MA 02142





Cites seven of my articles!

JACS
JOURNAL OF THE AMERICAN CHEMICAL SOCIETY

A good field for an enterprising assistant professor!

pubs.acs.org/JACS

Perspective

Optical Electrophysiology: Toward the Goal of Label-Free Voltage Imaging

Yuecheng Zhou, Erica Liu, Holger Müller, and Bianxiao Cui*

Cite This: *J. Am. Chem. Soc.* 2021, 143, 10482−10499

Read Online

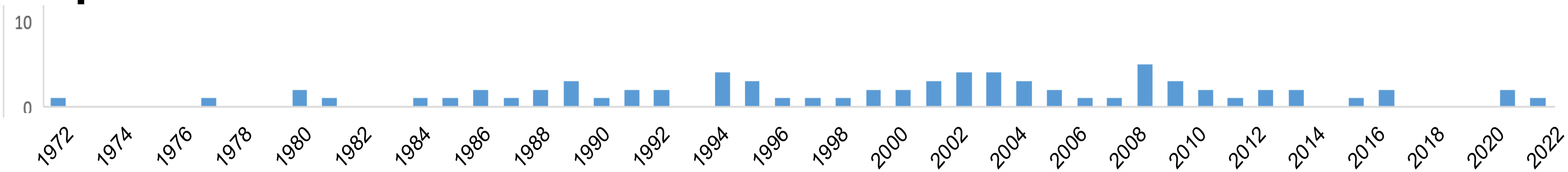
ABSTRACT: Measuring and monitoring the electrical signals transmitted between neurons is key to understanding the communication between neurons that underlies human perception, information processing, and decision-making. While electrode-based electrophysiology has been the gold standard, optical electrophysiology has opened up a new area in the past decade. Voltage-dependent fluorescent reporters enable voltage imaging with high spatial resolution and flexibility to choose recording locations. However, they exhibit photobleaching as well as phototoxicity and may perturb the physiology of the cell. Label-free optical electrophysiology seeks to overcome these hurdles by detecting electrical activities optically, without the incorporation of exogenous fluorophores in cells. For example, electrochromic optical recording detects neuroelectrical signals via a voltage-dependent color change of extracellular materials, and interferometric optical recording monitors membrane deformations that accompany electrical activities. Label-free optical electrophysiology, however, is in an early stage, and often has limited sensitivity and temporal resolution. In this Perspective, we review the recent progress to overcome these hurdles. We hope this Perspective will inspire developments of label-free optical electrophysiology techniques with high recording sensitivity and temporal resolution in the near future.

Table 1. Recent Advances in Label-Free Optical Electrophysiology

sensing mechanism	sensing methods	biological specimen	year	SNR	detection limit	signal bandwidth	near-field/ far- field detection
voltage-induced color change in electrochromic materials	ECORE	stem cell-derived cardiomyocyte, rat hippocampal neuron/brain slice	2020[60]	24−41	6.7 μV extracellular potential from single event	5 kHz, 300 Hz	near-field
action potential accompanied magnetic field	quantum diamond microscopy	worm and squid giant axon	2016[82]	>1	34 nT·μm$^{3/2}$·Hz$^{-1/2}$ magnetic field by averaging hundreds to thousands events	3.6 kHz	near-field
membrane deformation	AFM	mouse neurohypophysis	2007[95]	>25	5−10 nm deformation from single event	7 kHz	near-field
		lobster giant axon	2016[91]	N/A	<1 nm deformation by averaging 100 events	3 kHz	
	SPR	rat hippocampal neuron	2018[119]	7	<1 nm deformation from single event	1603 Hz	near-field
	interferometric imaging	HEK 293 cell	2012[101]	N/A	∼mrad phase change from single event	500 Hz	far-field
			2018[100]	47.7 dB	0.3 mrad/pixel phase change by averaging thousands events	1 kHz	
		rat cortical neuron	2017[106]	N/A	0.05 nm in optical path difference	200−300 Hz	
			2020[107]	21.5	4 pm/pixel deformation by averaging thousands events	10 kHz	
membrane scattering change	OCT/OCM	*Aplysia californica* bag cell neuron	2009[132]	N/A	single action potential by averaging 25 events	1 kHz (line scan rate)	far-field
	dark-field microscopy with nanoantenna	stem cell-derived cardiomyocyte	2019[133]	∼60	200 V/cm^2 potential from single event	1 kHz	near-field
membrane water molecules reorientation	SHG microscopy	mouse cortical neuron	2018[148]	4	long-term membrane depolarization from single event	1.67 Hz	far-field
membrane protein $-CH_3$ vibrational modes	SRS microscopy	mouse cortex neuron/brain slice	2017[153]	3.6	single action potential from single event	1 kHz (line scan rate)	far-field

Cardiac

- 1977 to the present
- 71 peer-reviewed journal articles, book chapters, review articles, reports, and issued patents

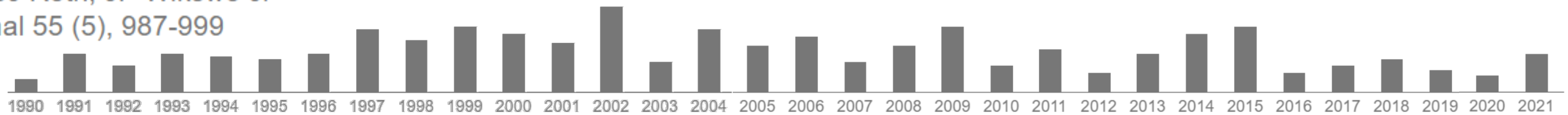


- For my Physics PhD, I went to Stanford in 1970 to use a vibrating inductance magnetometer and a superconducting magnetic shield to measure the magnetic field of the human brain.
- I built a very large mu-metal shield.
- I sold the superconducting shield's dewar for scrap.
- The vibrating inductance magnetometer was never completed.
- With the help of a friend and a technician, I built my own SQUID magnetometer/susceptometer.
- For my PhD, I made magnetic measurements of human cardiac electrical and magnetic activity.
- At Vanderbilt, I developed new cardiac measurements on dogs and people.
- I moved from people to dogs to rabbits because we could image the rabbit heart.

Current injection into a two-dimensional anisotropic bidomain 414 1989

NG Sepulveda, BJ Roth, JP Wikswo Jr

Biophysical journal 55 (5), 987-999



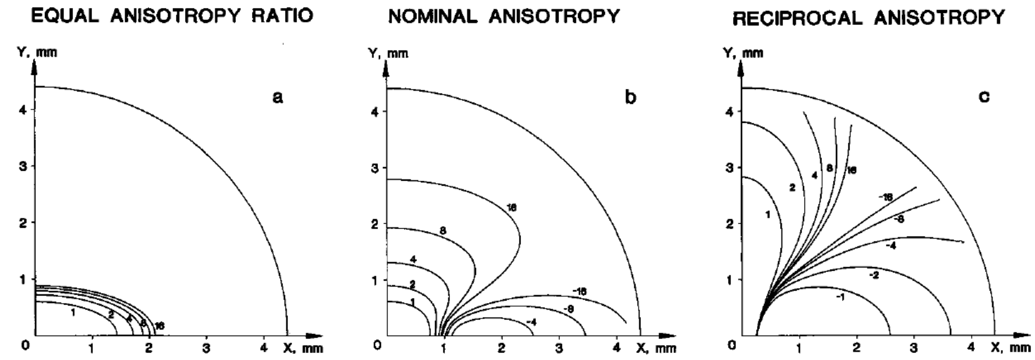


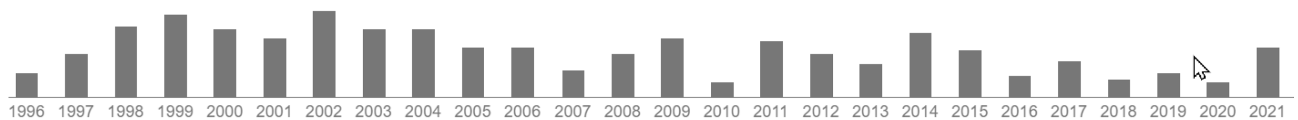
FIGURE 14 The +20 mV isopotential contour of the transmembrane potential for different amounts of injected current. The isopotential line is calculated for equal anisotropy ratios (*a*), nominal (*b*), and reciprocal conductivities (*c*). The current is applied extracellularly at the origin.

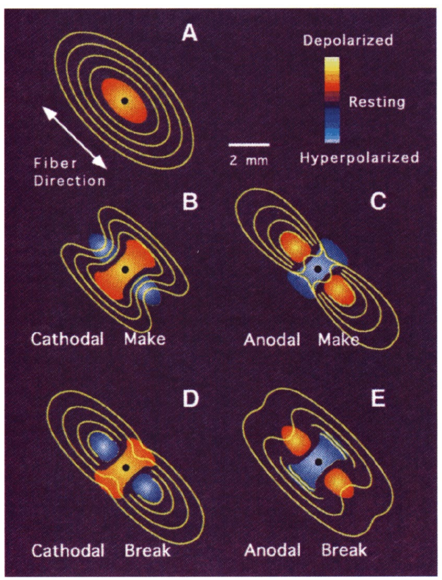
A good model for the magnetocardiogram converged with a fortuitous observation in the dog lab.

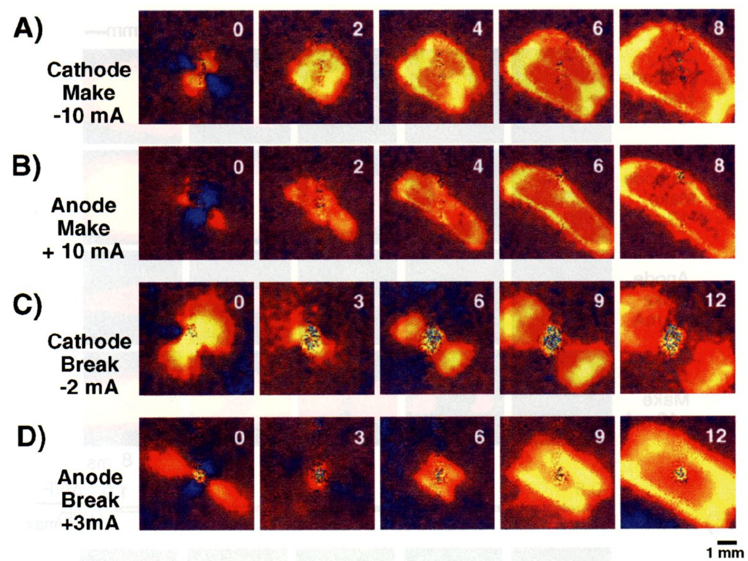
Virtual electrodes in cardiac tissue: a common mechanism for anodal and cathodal stimulation 418 1995

JP Wikswo Jr, SF Lin, RA Abbas

Biophysical journal 69 (6), 2195-2210

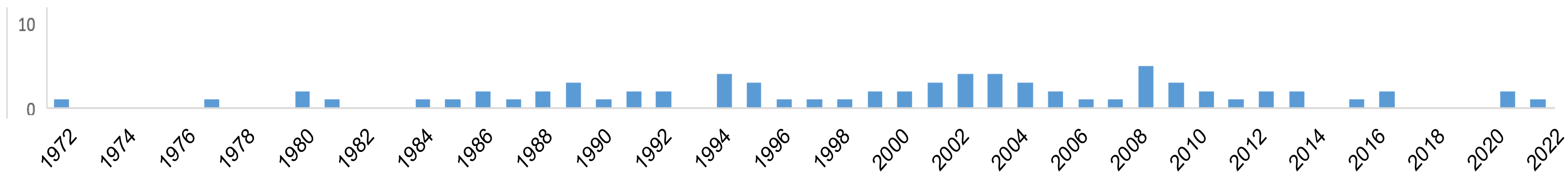






Cardiac

- 1977 to the present
- 71 peer-reviewed journal articles, book chapters, review articles, reports, and issued patents



I reduced my cardiac effort in ~2013 because…

- Brad Roth predicted and I had tested dozens of pieces of low-hanging theoretical fruit.
- Cardiac modeling became dominated by large groups with giant finite element codes far beyond my group's capabilities.
- NIH funding for cardiac electrophysiology contracted nationally.
- I could not find interested VUMC cardiac collaborators.
- I could not get NIH funding to move my rabbit heart work into cardiac metabolism.
- Organs-on-chips were shiny, fun, and well funded.
- I moved to heart-on-a-chip because my colleagues and I figured out how to measure something others couldn't.

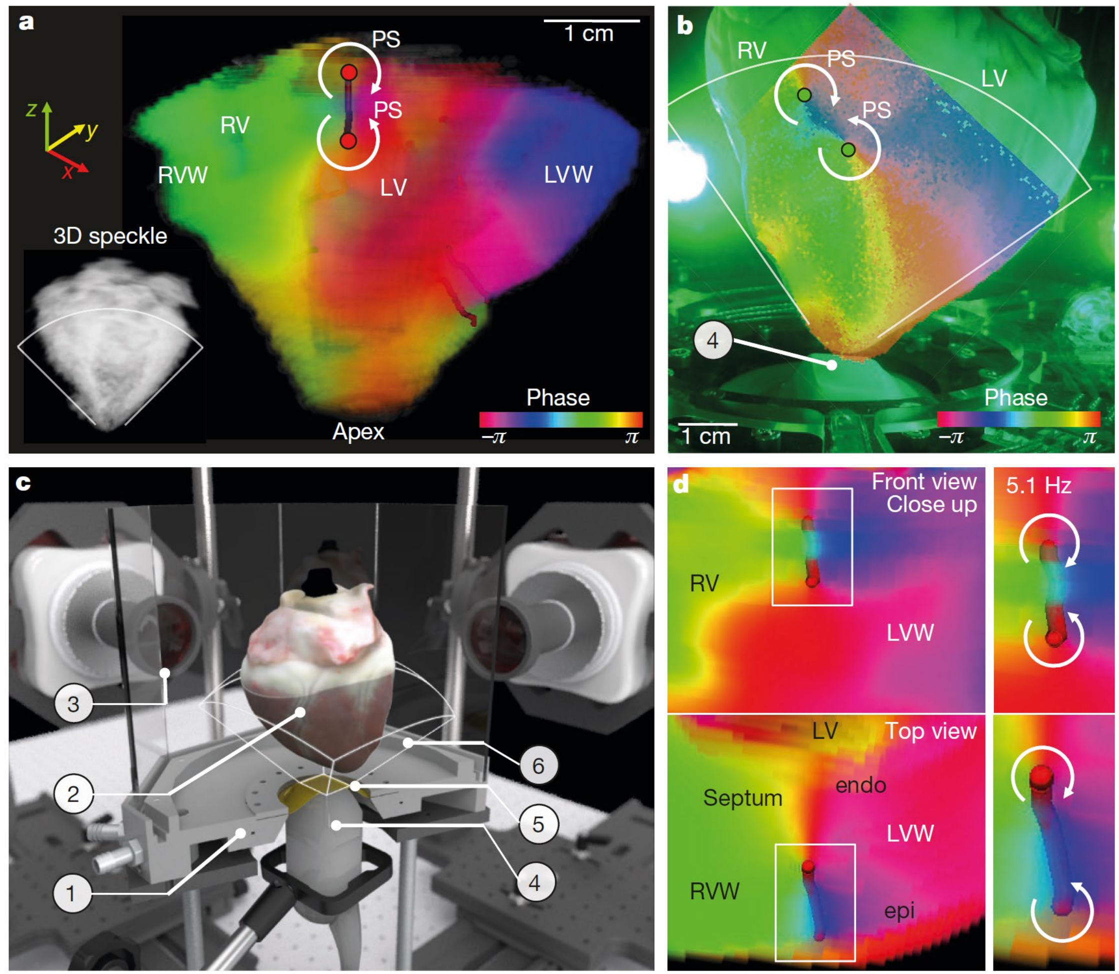
LETTER

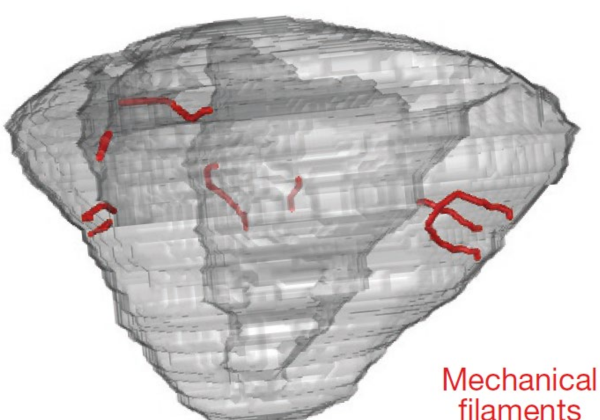
doi:10.1038/nature26001

Electromechanical vortex filaments during cardiac fibrillation

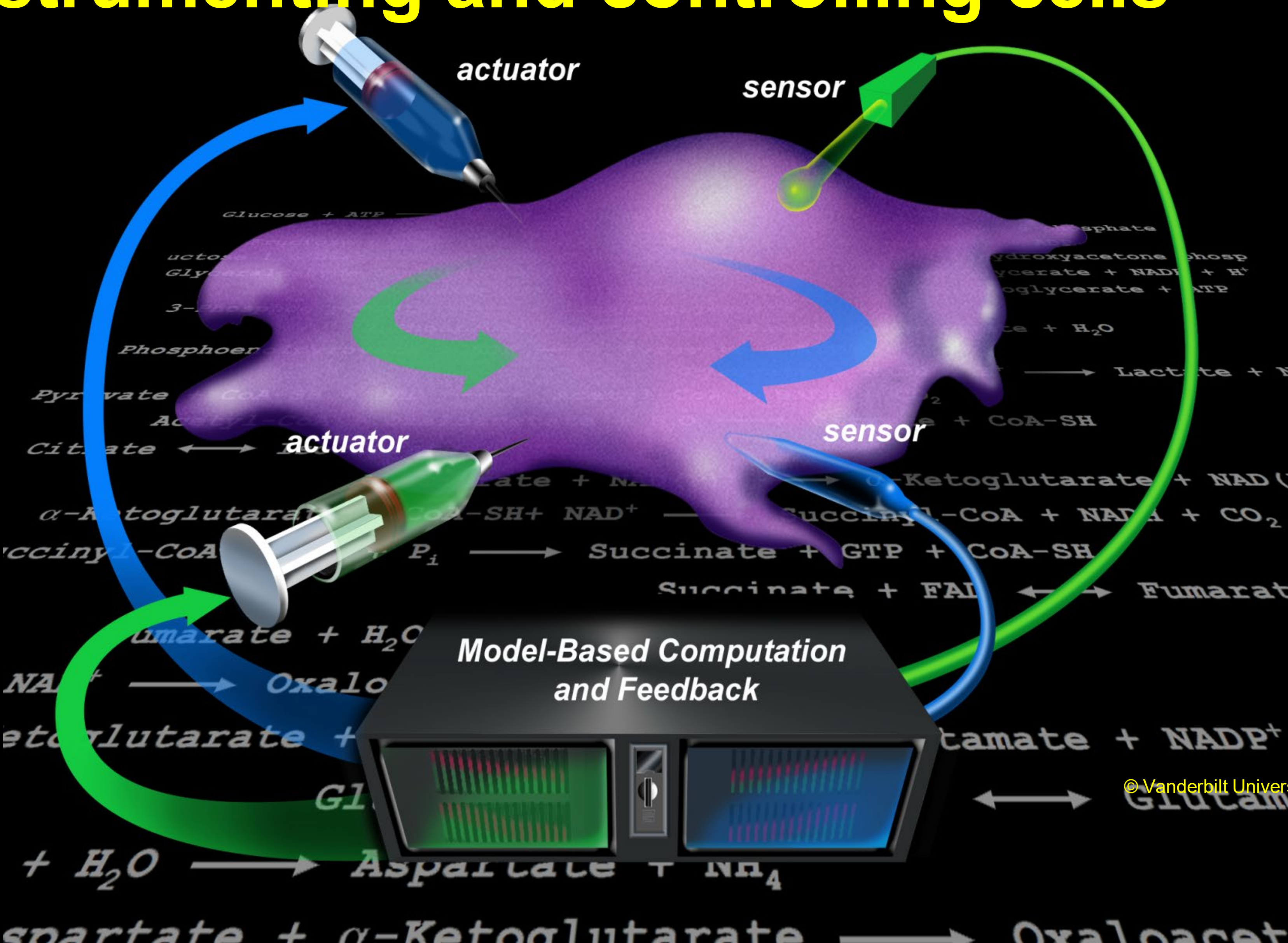
J. Christoph[1,2,3], M. Chebbok[2,4], C. Richter[1,2,4], J. Schröder-Schetelig[1,2,3], P. Bittihn[5], S. Stein[1,3], I. Uzelac[6], F. H. Fenton[6], G. Hasenfuß[2,4], R. F. Gilmour Jr[7] & S. Luther[1,2,3,8,9,10]

Figure 1 | Measurement of intramural mechanical filament-like phase singularity. a, Double scroll wave (phase) and U-shaped mechanical filament (red) recorded at 134 volumes per second during ventricular tachycardia inside the left ventricular wall (LVW) of a contracting Langendorff-perfused pig heart using 4D ultrasound (Supplementary Video 1 and Extended Data Fig. 1 a, b). LV, left ventricle; RV, right ventricle; RVW, right ventricular wall; PS, phase singularity. **b**, Figure-of-eight spiral wave (membrane voltage) on the surface of the left and right ventricle with two phase singularities obtained by recording optical mapping data at the same time as the recording shown in **a**. The ultrasound transducer is indicated by (4); the white lines indicate the field of view. **c**, Schematic of the experimental setup. (1) temperature-controlled perfusion bath; (2) Langendorff-perfused pig heart; (3) high-speed EMCCD(electron-multiplying charge-coupled device) cameras (only two shown) and LED illumination (not shown); (4) 4D ultrasound transducer; (5) acoustic window (membrane); (6) 3D field of view of ultrasound transducer. See the Methods for details. **d**, Detail (front and top view) of the U-shaped mechanical filament (red) of the scroll wave shown in **a**.



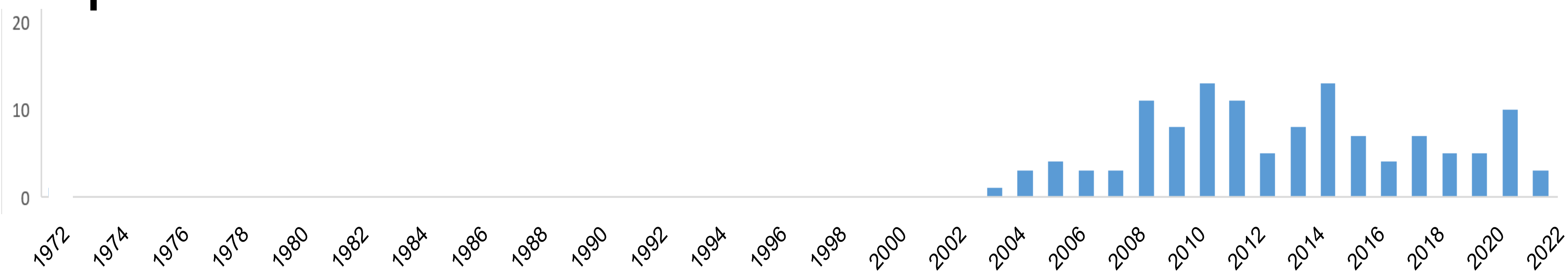


VIIBRE 2001
Instrumenting and controlling cells



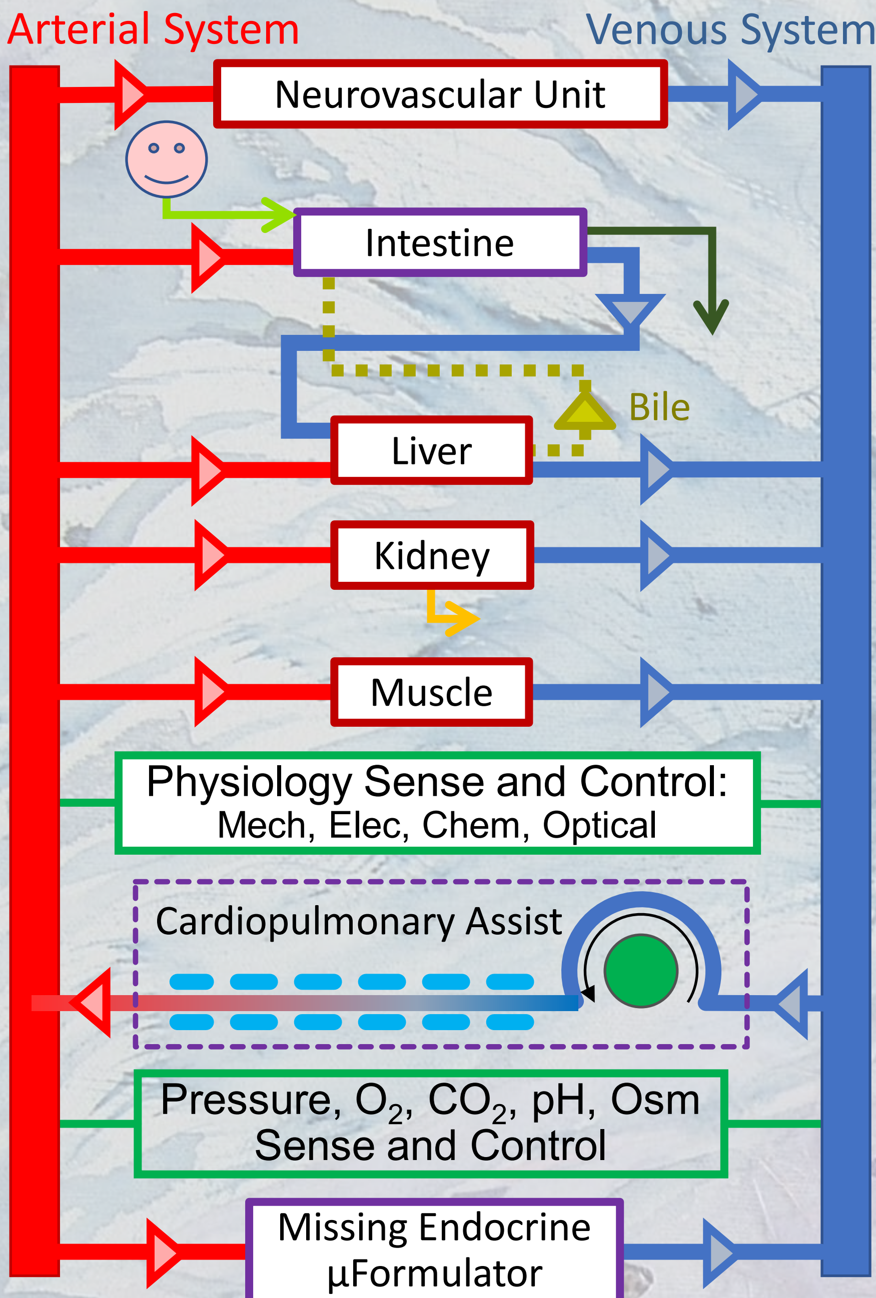
MicroFluidics, Systems Biology, and Organs-on-Chips

- 2002 to the present
- 123 peer-reviewed journal articles, book chapters, review articles, reports, and issued patents

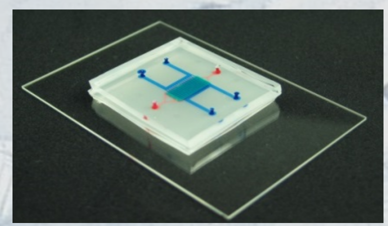


- In 2000, David Piston and I agreed that Vanderbilt's biological physics program needed to establish by 2010 an international presence in microfluidics for biology.
- I entered the field in 2001 with a $5.5 million dollar Vanderbilt Academic Venture Capital Fund grant to create the Vanderbilt Institute for Integrative Biosystems Research and Education (VIIBRE).

NIH-NCATS MPS Integration

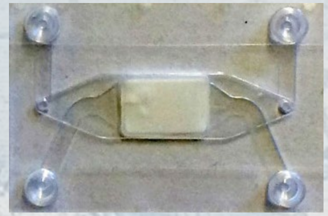


NVU



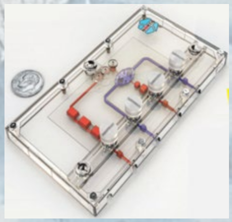
Vanderbilt

Intestine



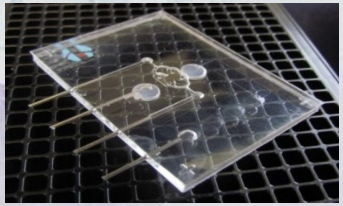
Hopkins, Baylor

Liver



Pittsburgh

Kidney



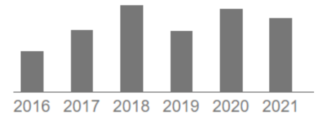
Washington

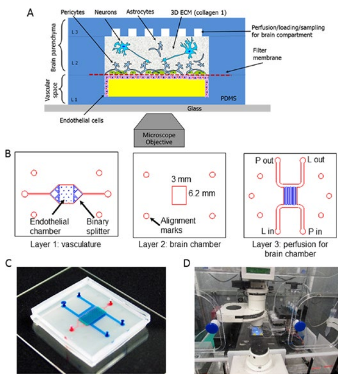
ME-µF

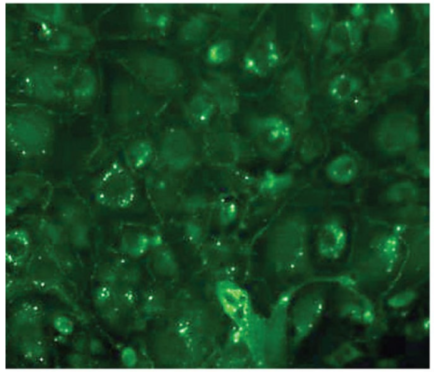
Vanderbilt

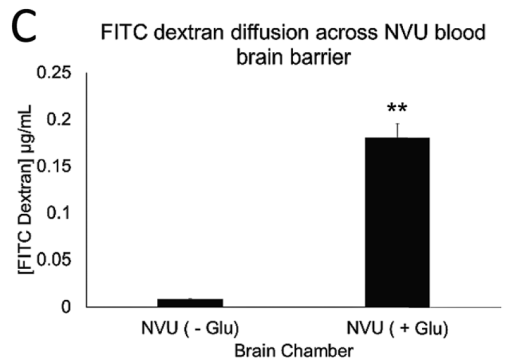
Recreating blood-brain barrier physiology and structure on chip: A novel neurovascular microfluidic bioreactor 283 2015

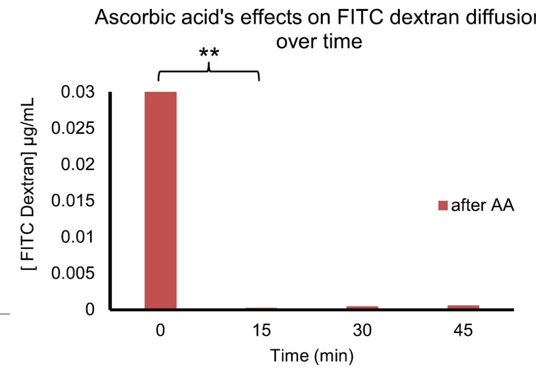
JA Brown, V Pensabene, DA Markov, V Allwardt, MD Neely, M Shi, ...
Biomicrofluidics 9 (5), 054124





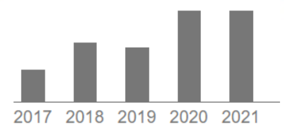


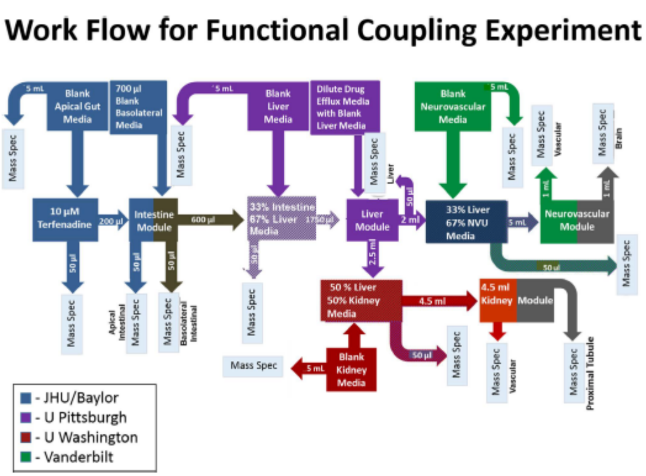


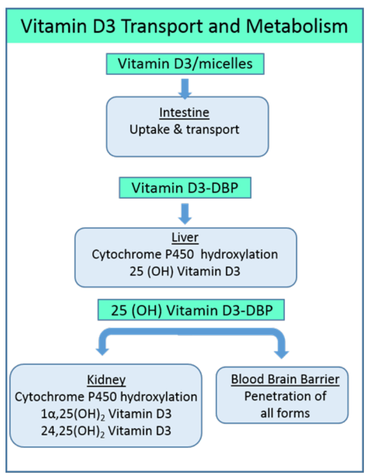


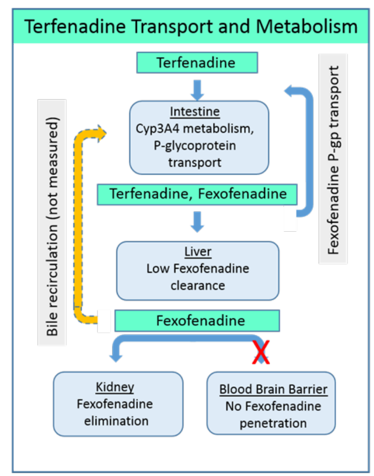
Functional coupling of human microphysiology systems: intestine, liver, kidney proximal tubule, blood-brain barrier and skeletal muscle 162 2017

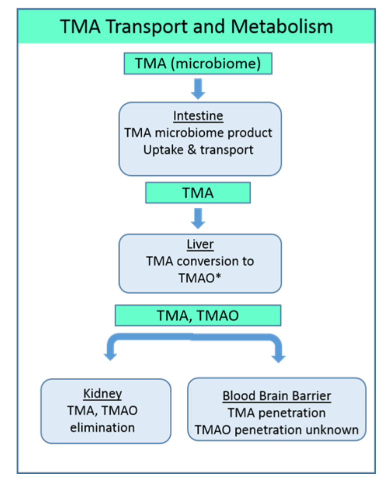
L Vernetti, A Gough, N Baetz, S Blutt, JR Broughman, JA Brown, ...
Scientific reports 7 (1), 1-15









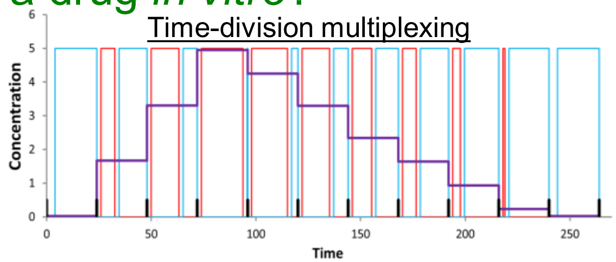


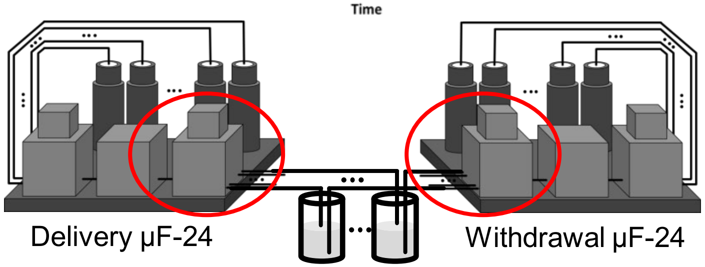
The first prediction made by an *in vitro* organ-chip model that was confirmed by measurements on humans.

Multi-MicroFormulators for testing the effects of drug timing

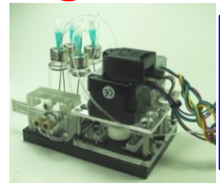
VI∫BRE

- Matt Wagoner – "Your missing-organ μF is great, but I need 96 channels."
- What can you learn by lengthening or shortening the <u>effective</u> PK profile of a drug *in vitro*?

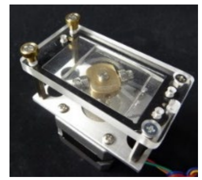


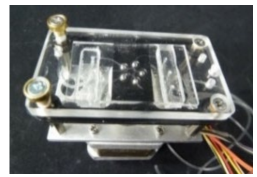


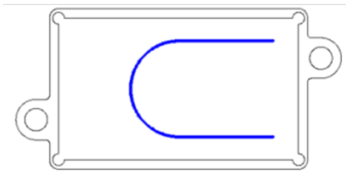
- What is the optimal timing for repeated or multi-drug dosing?

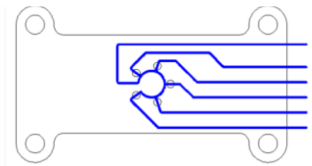


- Request: May 2015
- Contract: October 2015
- Delivery: January 2016

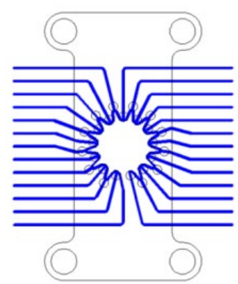


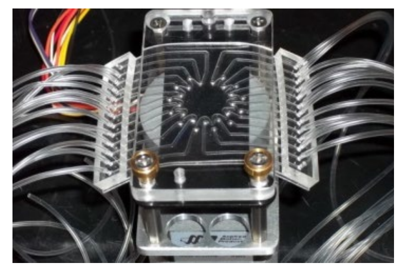


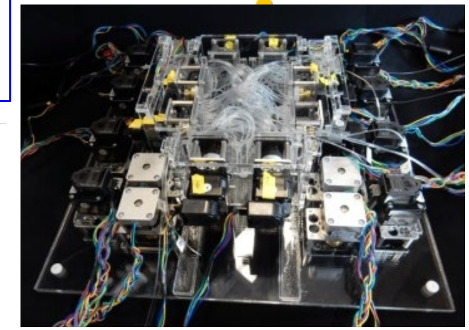


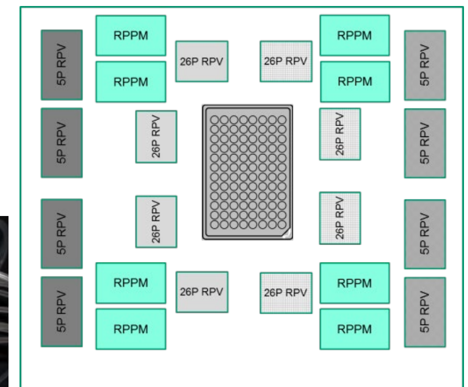


Voilà – a 25 port valve!



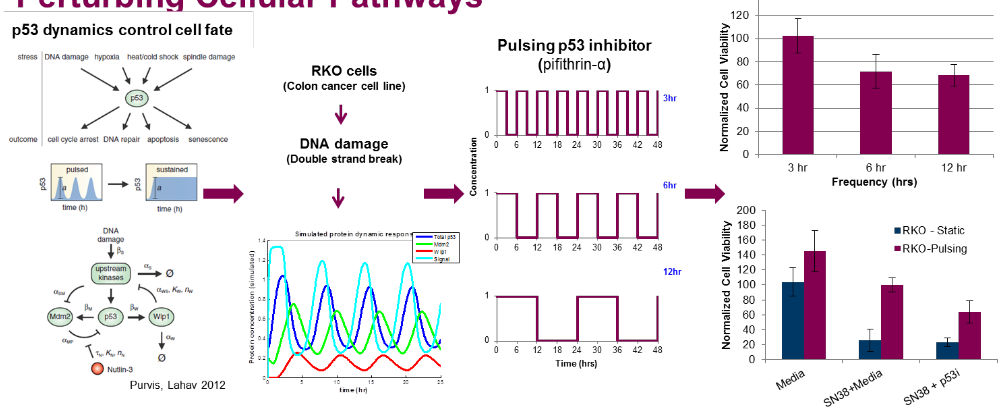




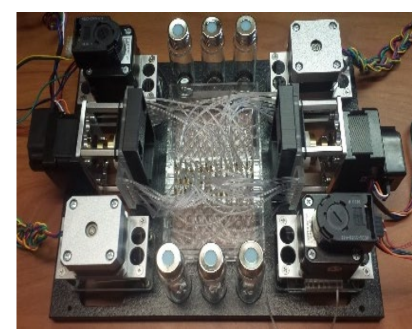


Funded by AstraZeneca. First in operation at AZ - Waltham, MA January, 2016

Perturbing Cellular Pathways



Funded by AstraZeneca and NIH-NCATS/CDFRC



2016-2018

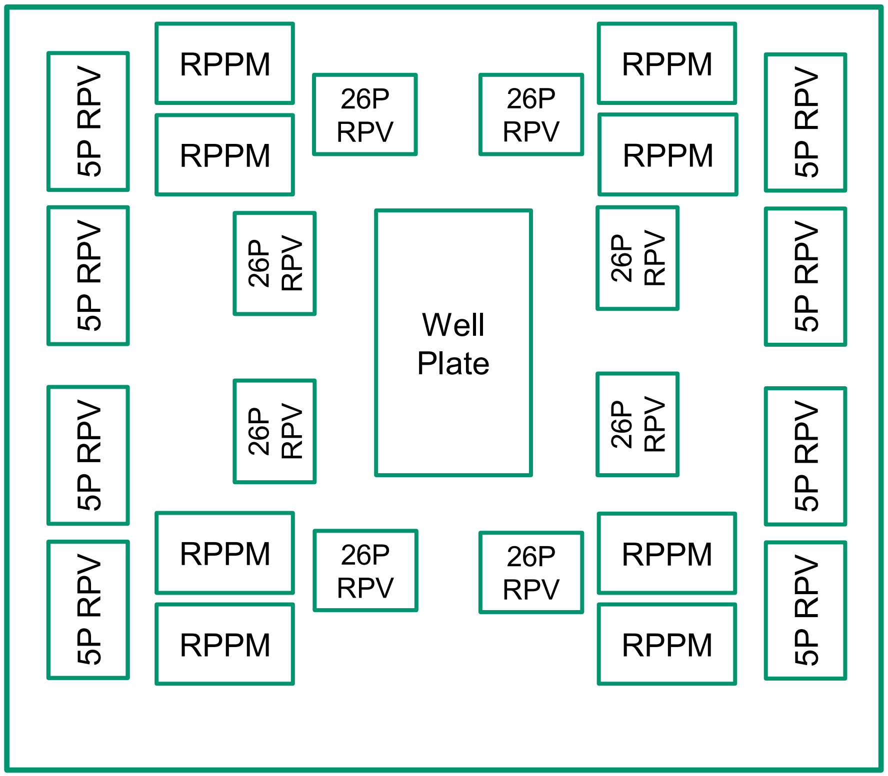
Patents issued and pending

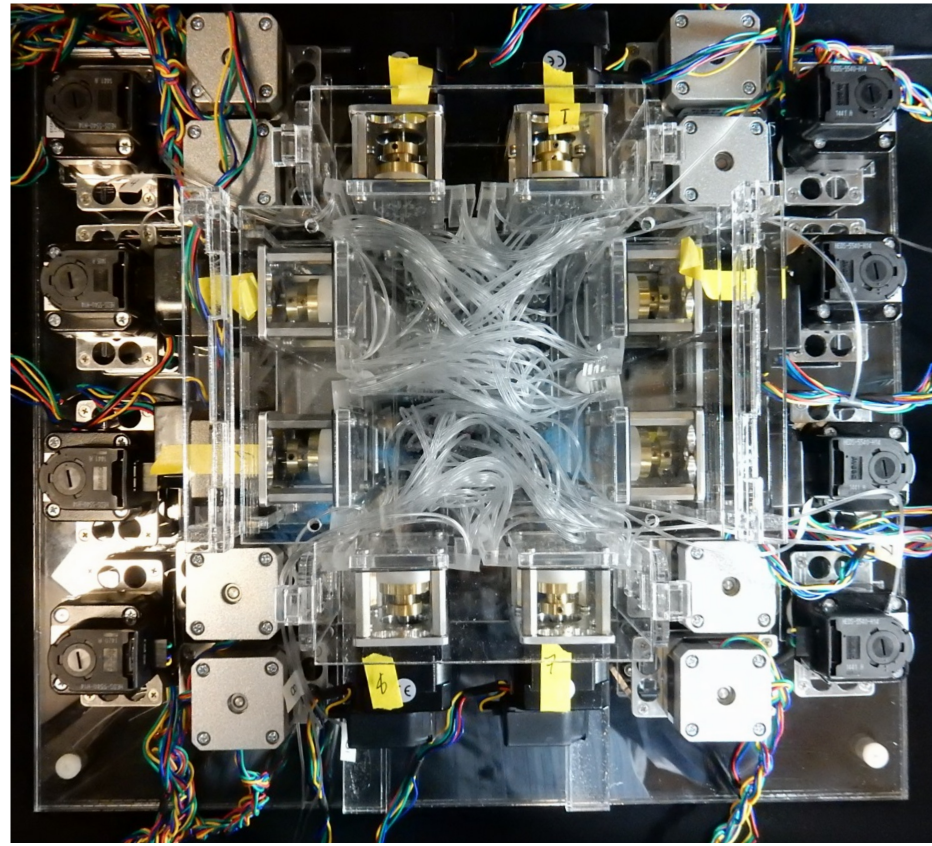
- Currently performing additional experiments to understand signaling dynamics and its influence on cell fate

Courtesy of Aditya Kolli, Harish Shankaran, Matthew Wagoner, and Jay Mettetal, AstraZeneca

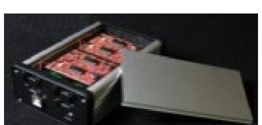
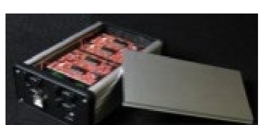
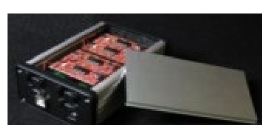
VIIBRE’s µF-96 v1.0: January 2016

Funded in part by AstraZeneca as a collaborative effort initiated by Matt Wagoner, with Jay Mettetal and postdoc Aditya Kolli. Now involving Kristin Fabre and Clay Scott, and postdocs Sudhir Deosarkar and Jingwen Zhang.





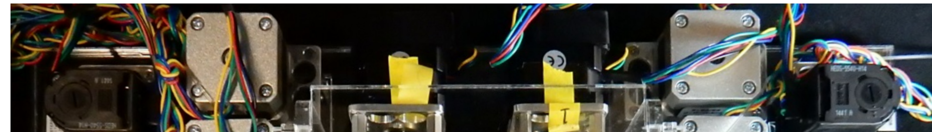


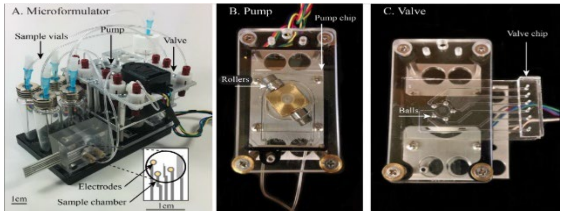
Use time-division multiplexing to individually formulate, deliver, and remove custom media cocktails to each well of a 96-well plate to simulate PK profiles.

VIIBRE's µF-96 v1.0: January 2016

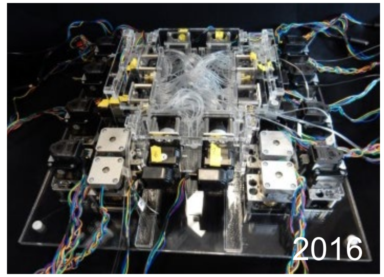
Funded in part by AstraZeneca as a collaborative effort initiated by Matt Wagoner, with Jay Mettetal and postdoc Aditya Kolli. Now involving Kristin Fabre and Clay Scott, and postdocs Sudhir Deosarkar and Jingwen Zhang.

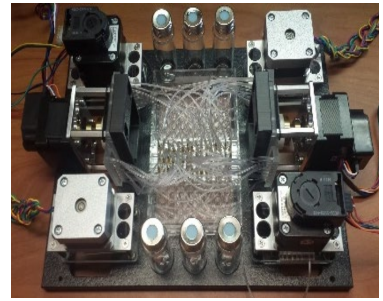


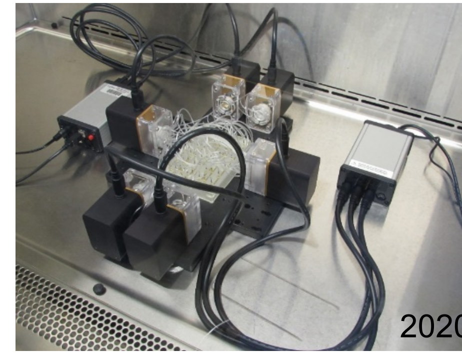
The VIIBRE MicroFormulator

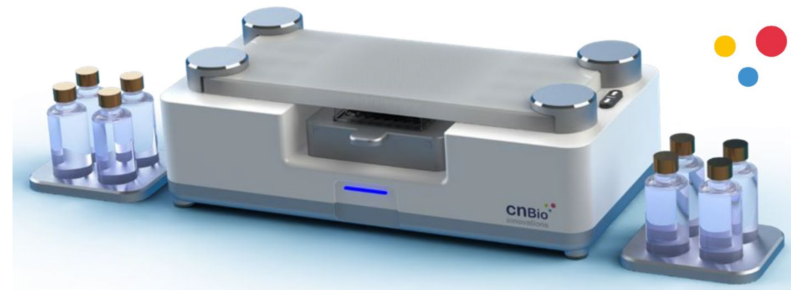


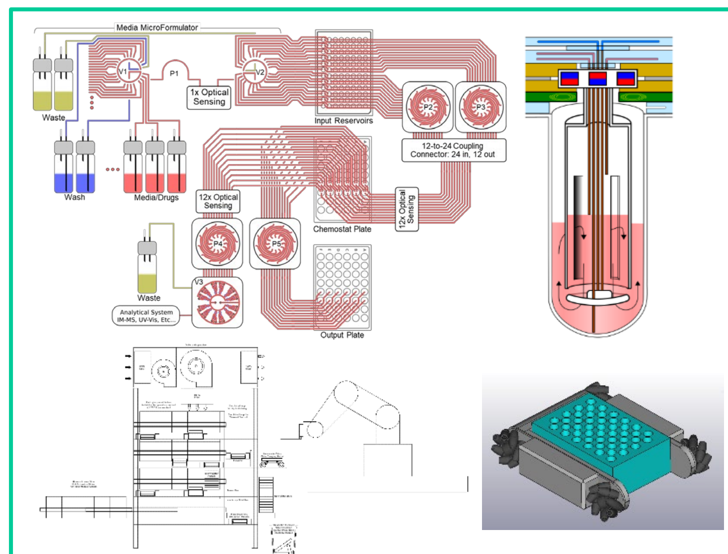
2013











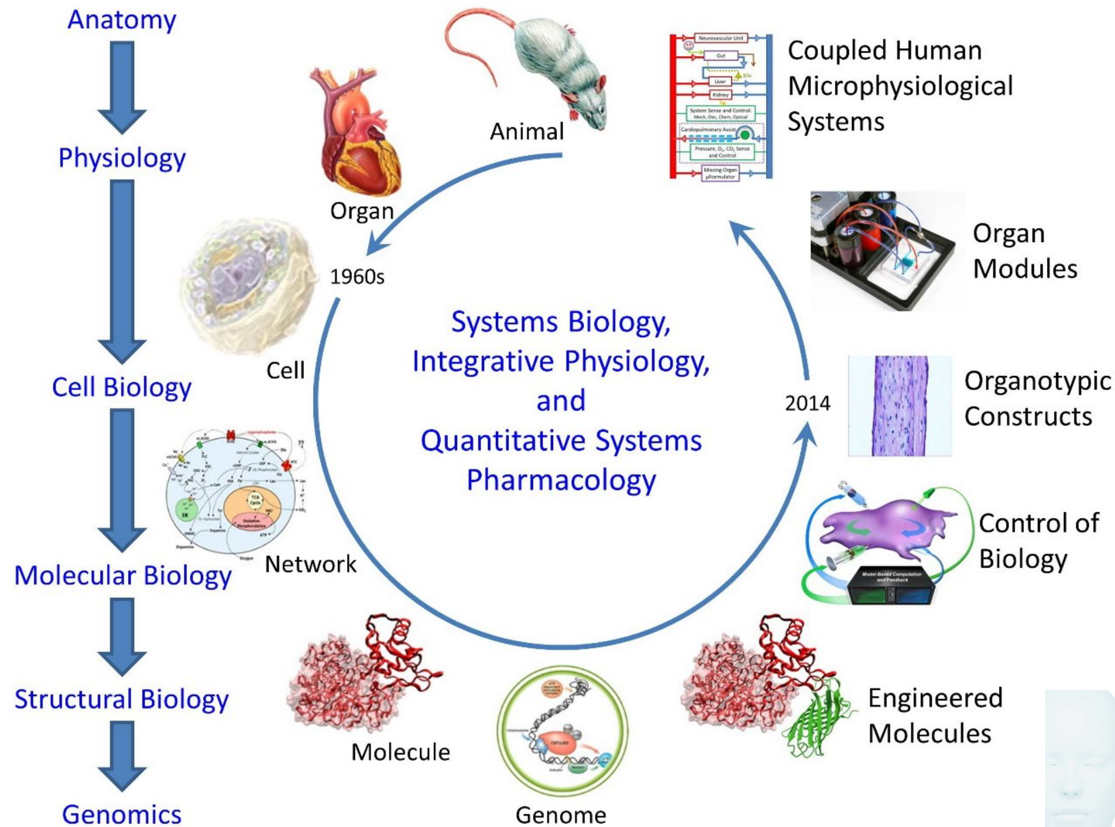
The CN Bio Innovations PhysioMimix PK!

October 5, 2021: https://cn-bio.com/cn-bio-expands-service-offering-to-support-oncology-drug-discovery/

Tomorrow

The Complexity of Biology

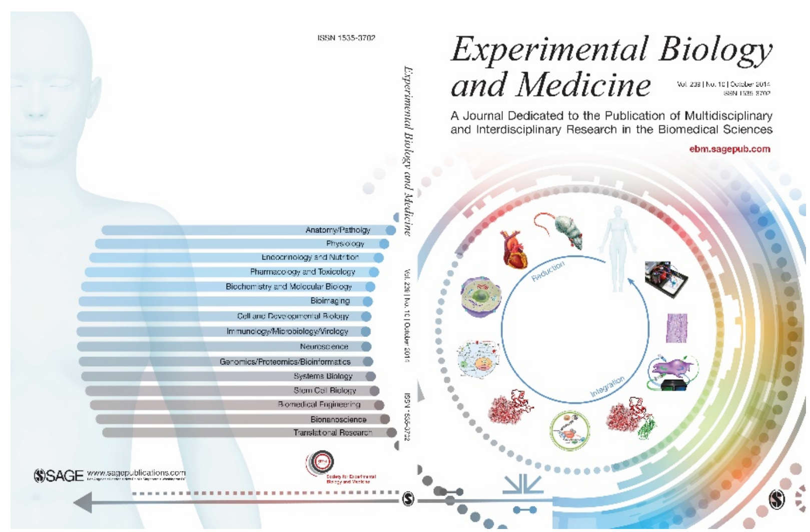
Closing the Hermeneutic Circle of Biology



Wikswo, Experimental Biology and Medicine 2014; 239: 1061–1072

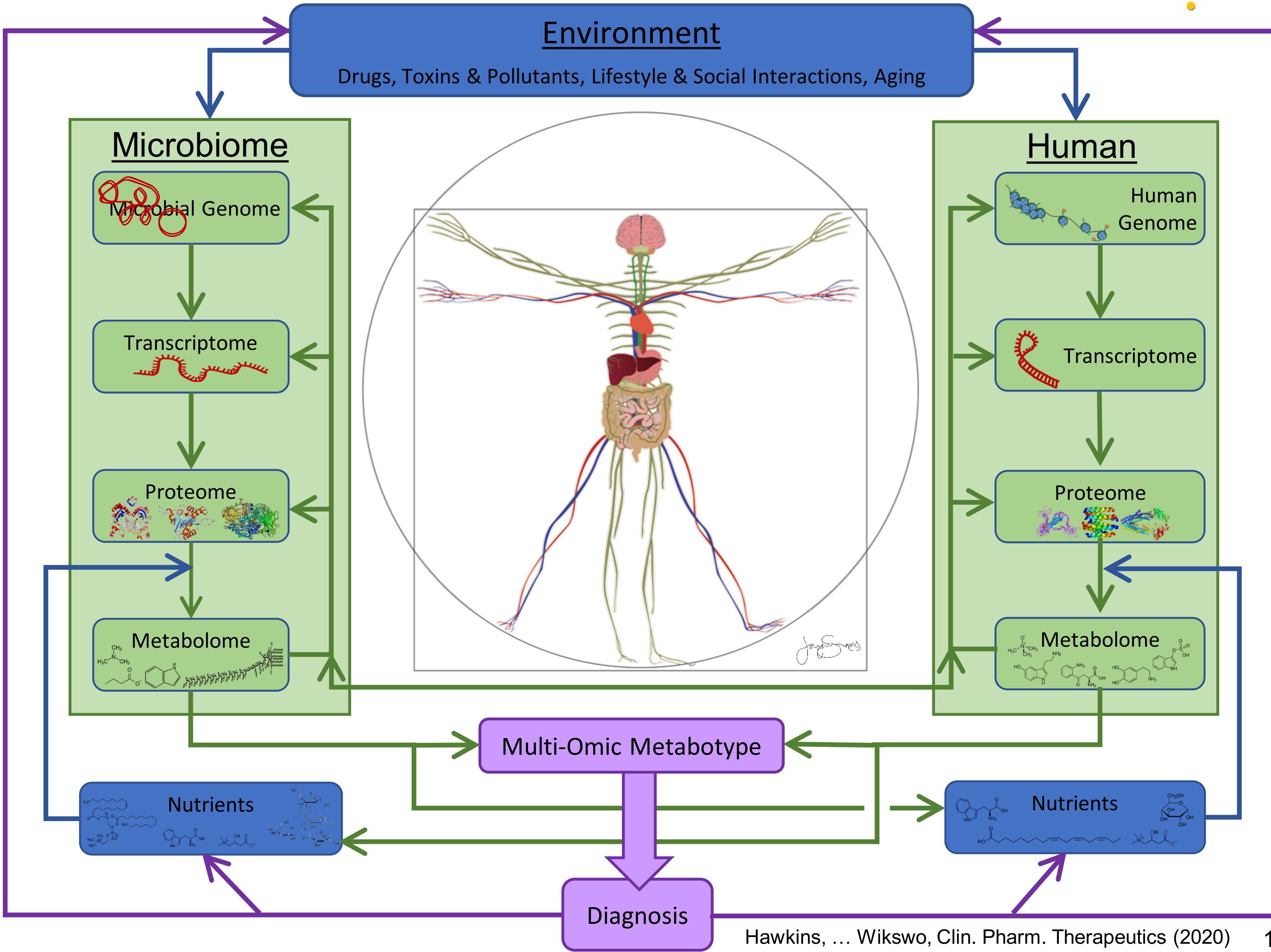
Hermeneutic Circle: You cannot understand the whole until you understand the parts. You can't understand the parts until you understand the whole.

EBM's Permanent Cover



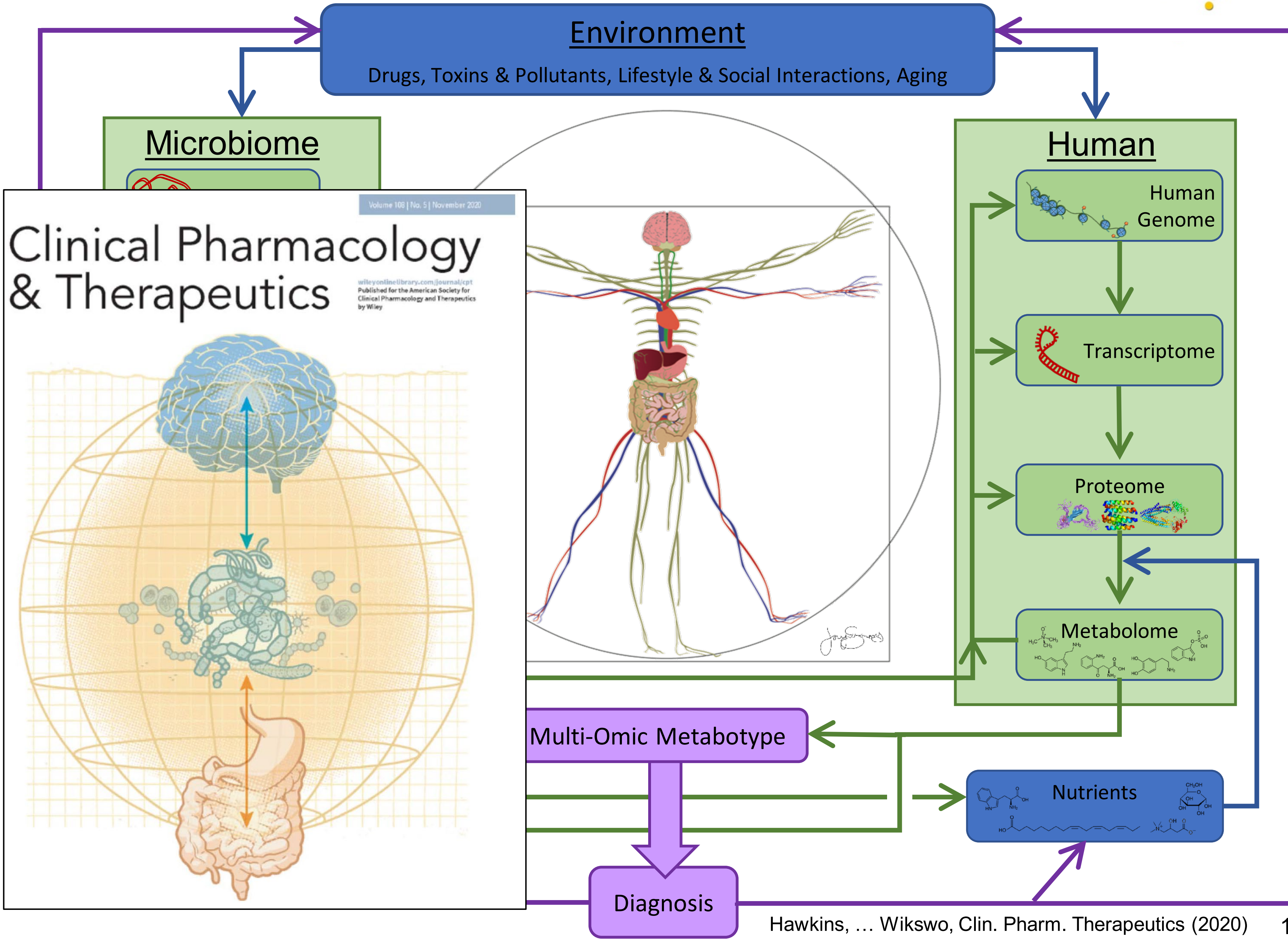
Wikswo and Porter, Experimental Biology and Medicine 2015; 240: 3–7

Microbiome-Gut-Liver-Brain Axis



Hawkins, … Wikswo, Clin. Pharm. Therapeutics (2020)

Microbiome-Gut-Liver-Brain Axis

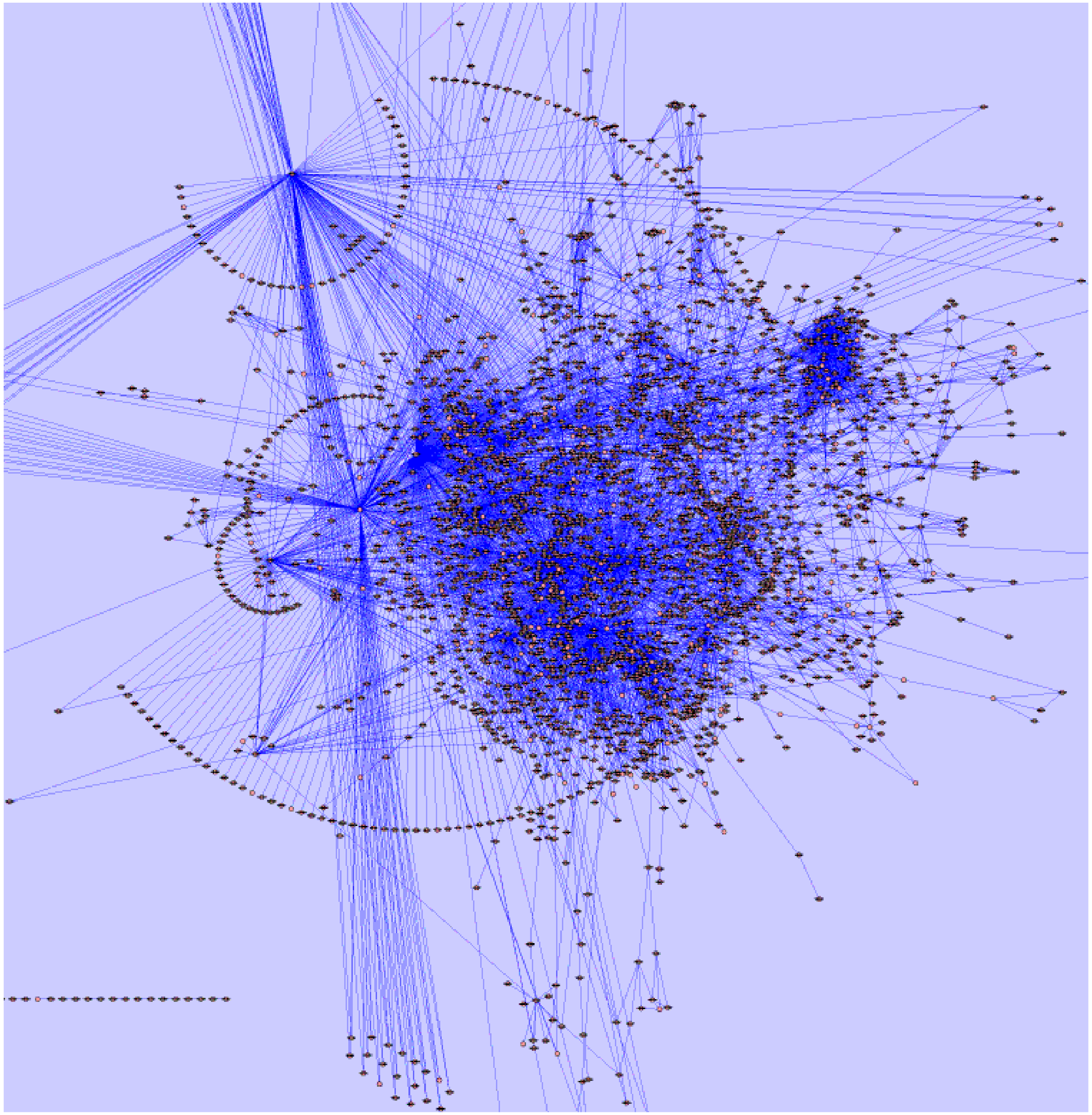


Hawkins, … Wikswo, Clin. Pharm. Therapeutics (2020)

A Really Hard Problem:
Metabolic and Signaling Kinetics in a Multiscale Environment

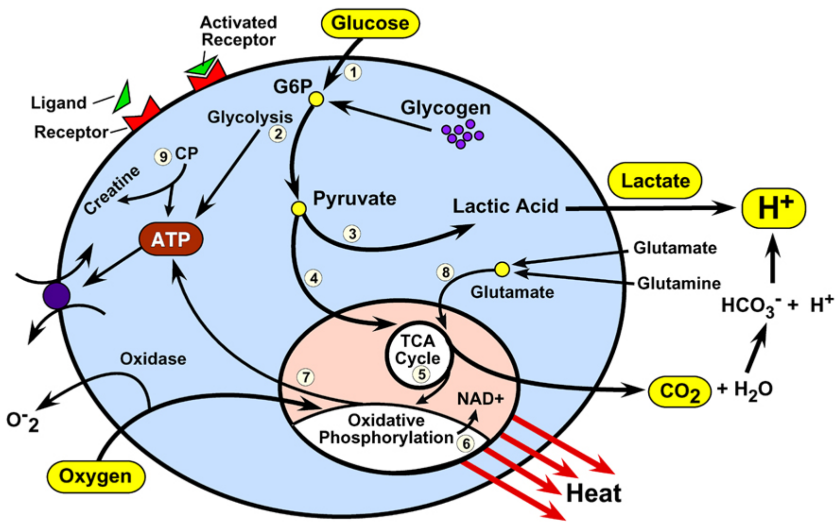
- Question:
  - How do we describe and interpret biological complexity over multiple spatiotemporal scales?
- The standard solution:
  - Genomics, proteomics, transcriptomics…
  - Reductionist analysis of components
  - Mathematical modeling….

Yeast Interactome

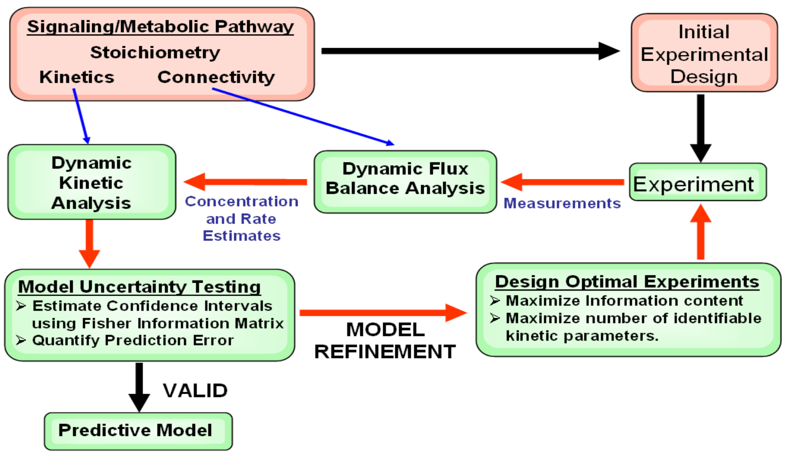


The Models

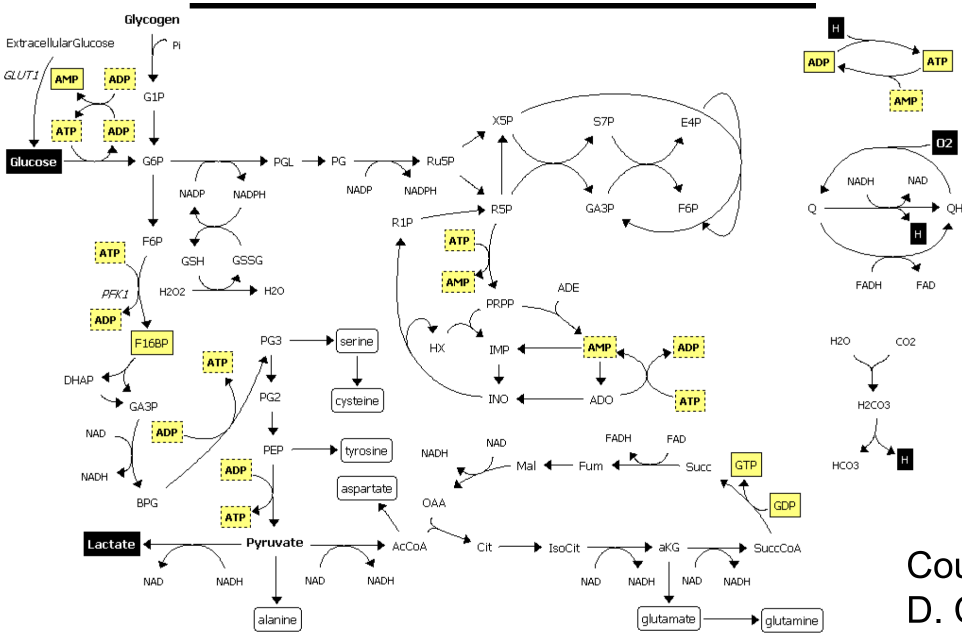
Effective Models



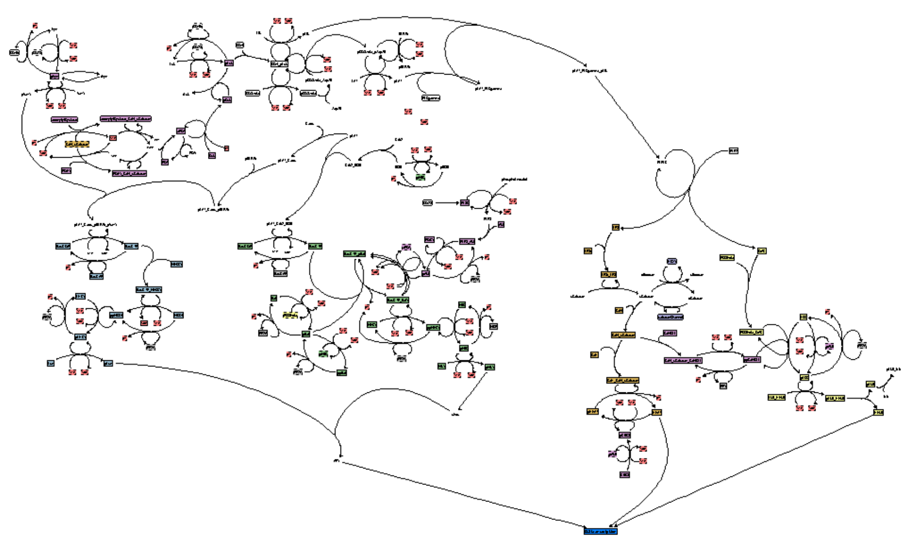
Algorithmic Framework



Central Carbon Metabolism

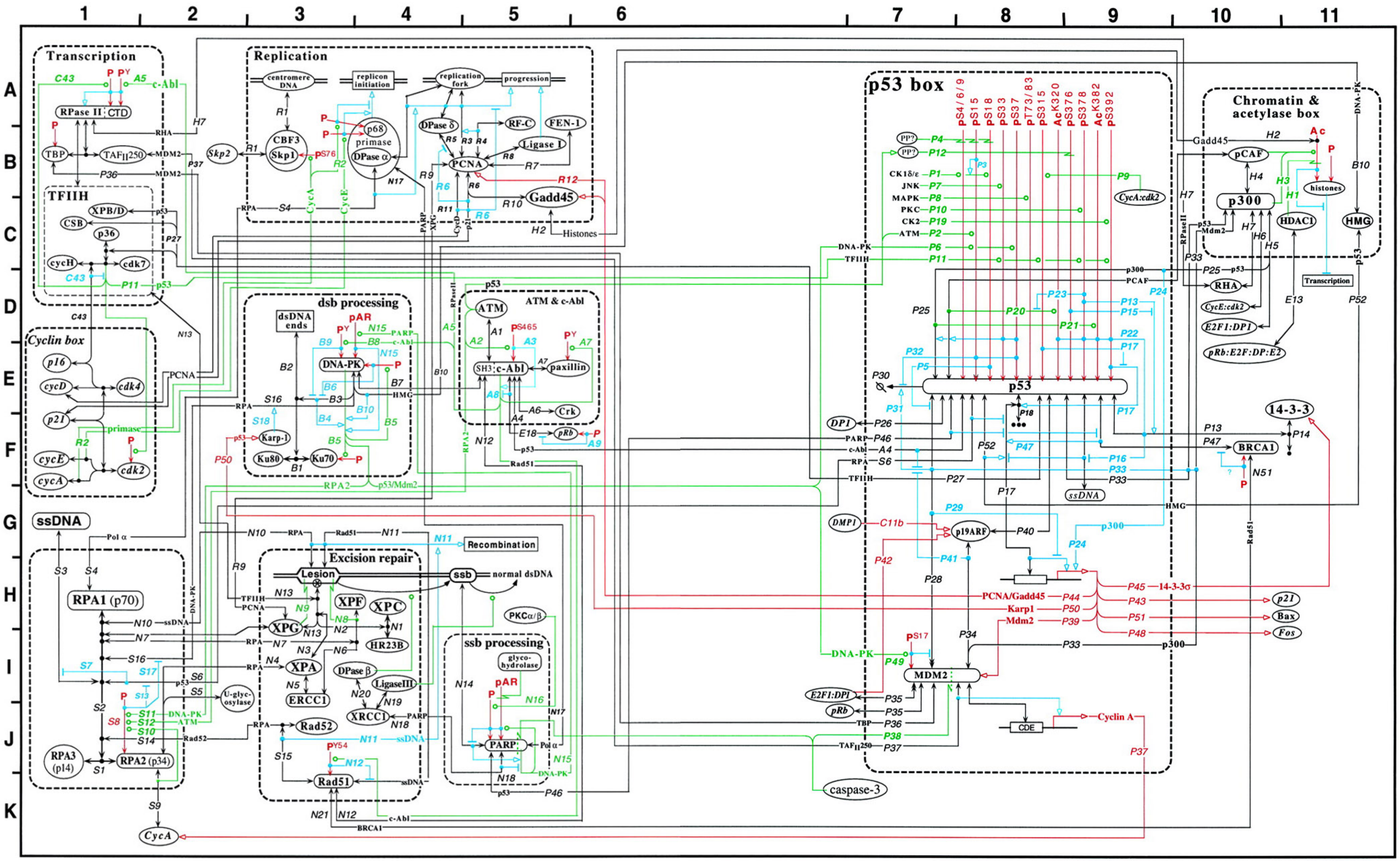


T-cell Signaling



Courtesy of S. Sundaram and Jerry Jenkins, CFDRC, D. Cliffel, Vanderbilt

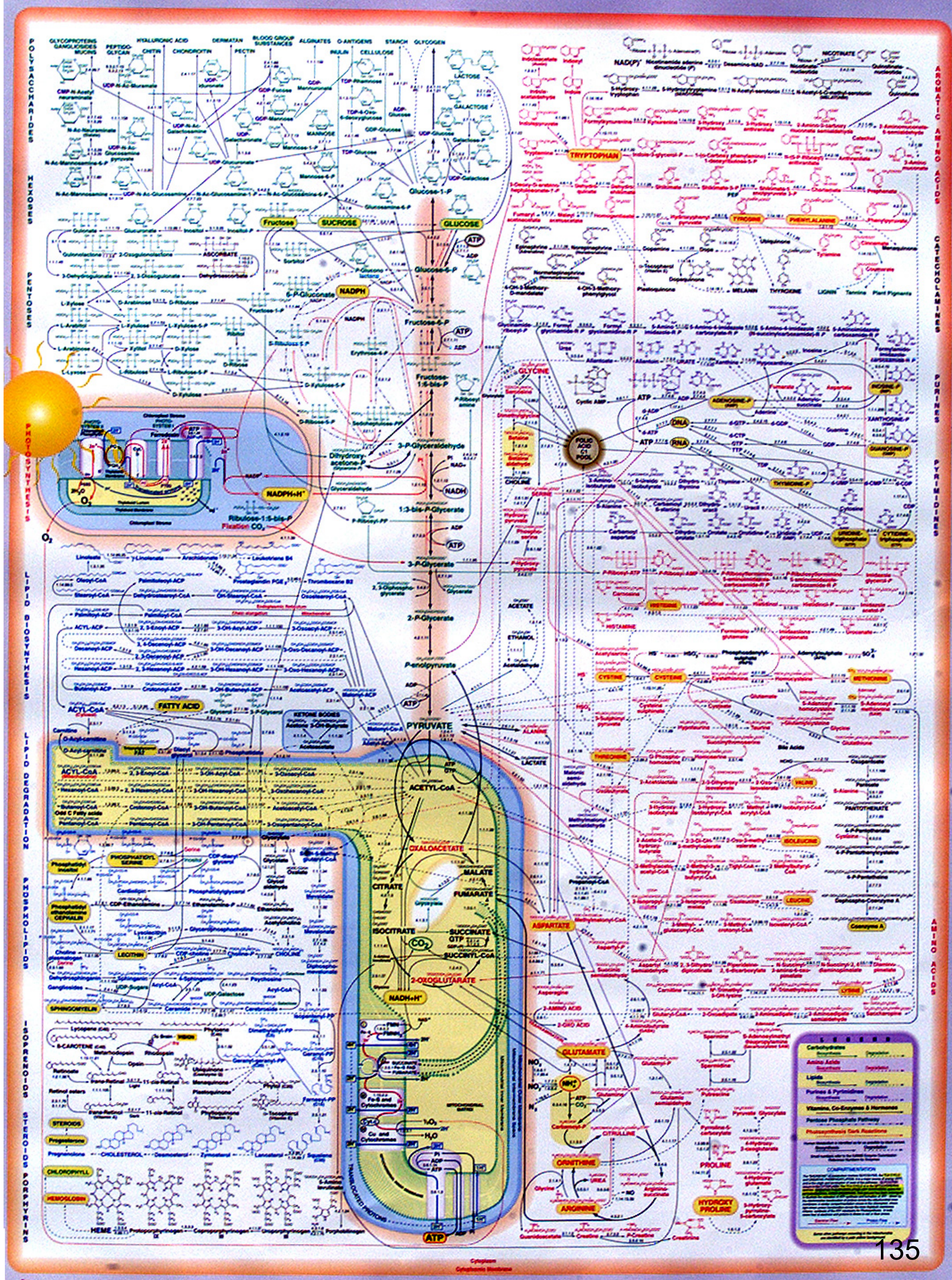
Molecular Interaction Map: DNA Repair



KW Kohn, “Molecular Interaction Map of the Mammalian Cell Cycle Control and DNA Repair Systems,” *Mol. Biol. of the Cell*, 10: 2703-2734 (1999)

'Postgenomic' Integrative/Systems Physiology/Biology

- Suppose you wanted to **calculate** how the cell responds to a toxin…
  - Specify concentrations and
  - Rate constants
  - Add gene expression,
  - Protein^N interactions, and
  - Signaling pathways
  - Time dependencies
  - Include intracellular spatial distributions, diffusion, and transport: ODE → PDE(t)
  - … and then you can **calculate** how the cell behaves in response to a toxin



A <u>Really Hard</u> Problem

If the human brain were so simple
that we could understand it,
we would be so simple
that we couldn't.

Emerson M. Pugh, 1938

Yet one more Really Hard Problem

Pugh's observation applies to biology:

Human biology may be too complicated for humans to fully comprehend.

John Wikswo

The Practical Problem

- "Exact" modeling of a single mammalian cell may require >100,000 *dynamic* variables and equations, maybe >1,000,000
- Cell-cell interactions are critical to system function
- 10^9 - 10^{11} interacting cells in some organs
- Cell signaling involves highly *DYNAMIC* biochemical cascades with positive and negative feedback
- Multiple, overlapping regulatory mechanisms
- Many of the interactions are nonlinear
- Models might have a Leibnitz (1 L = N_a) of PDEs
- **The data don't yet exist to drive the models**

It's the numbers….

Where do we get a mole of numbers?

Dennis Bray understands the problem….

- “The past few decades have seen such an explosion of knowledge about the contents of living cells that we now swim in an ocean of data.”

  D. Bray. Reductionism for biochemists: how to survive the protein jungle. *Trends Biochem.Sci.* 22 (9):325-326, 1997.

- “How can we come to terms intellectually with such an enormous number of interacting entities?”

A possible failure mode

Ontological failure: The phenomenon you are interested in requires elements or laws outside of the set you have been given.

D. Bray. Reductionism for biochemists: how to survive the protein jungle. *Trends Biochem.Sci.* 22 (9):325-326, 1997.

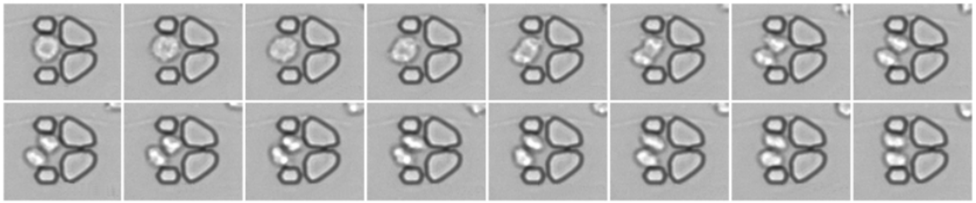
The solution to ontological failure

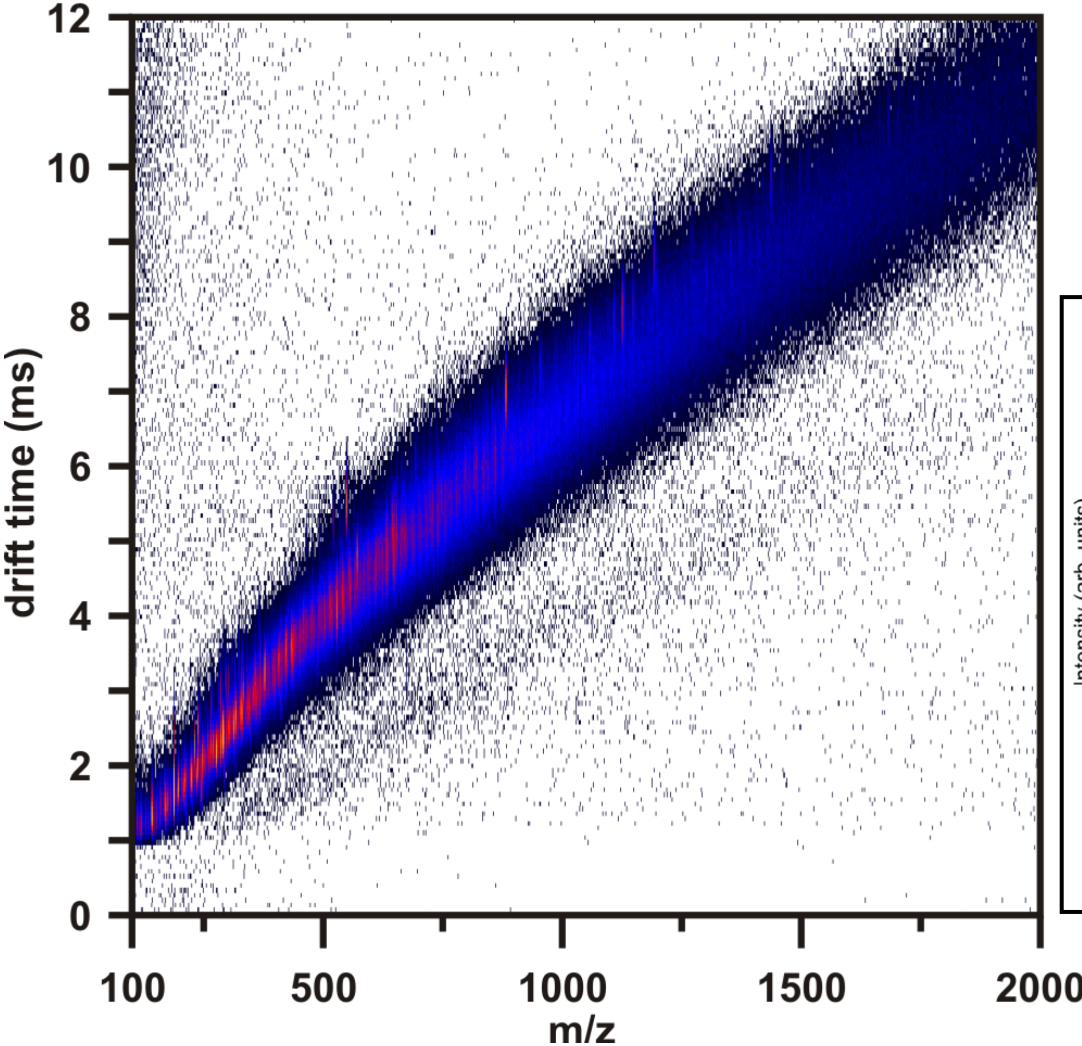
Get more data…

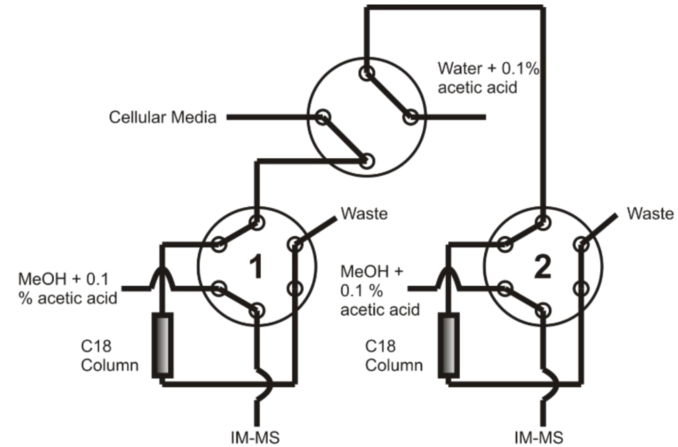
The Practical Problem

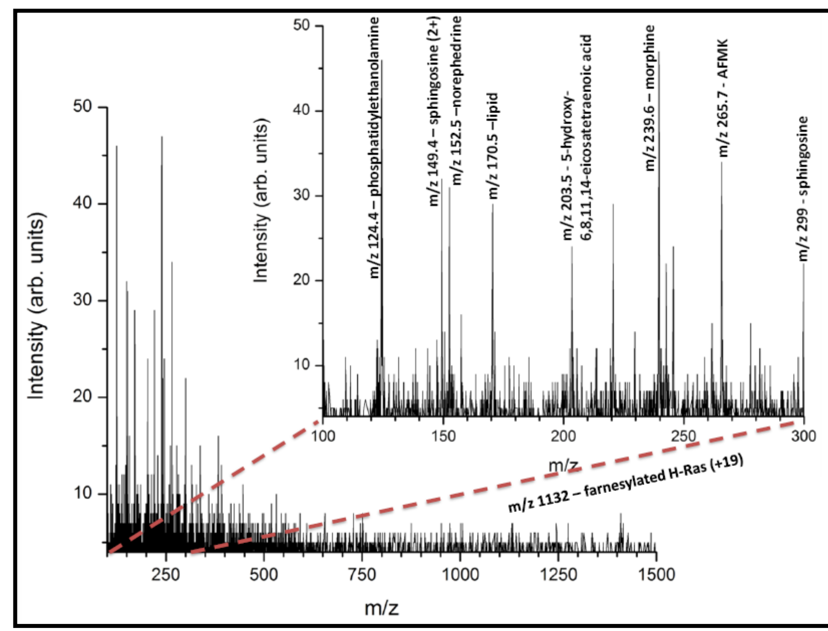
- Modeling of a single mammalian cell may require >100,000 *dynamic* variables and equations, maybe > 1,000,000
- Cell-cell interactions are critical to system function
- 10^9 - 10^{11} interacting cells in some organs
- Cell signaling involves highly *DYNAMIC* biochemical cascades with positive and negative feedback
- Multiple, overlapping regulatory mechanisms
- Many of the interactions are nonlinear
- Models might have a Leibnitz (1 L = N_a) of PDEs
- **The data don't yet exist to drive the models**
- Hence we need to **experiment…**

Real-time desalting enables on-line IM-MS spectra from trapped Jurkat cells









Images from Jeff Enders and John McLean, Vanderbilt

How do you deal with a Leibnitz of non-sparse PDEs involving 100,000 nonlinear variables?

Carefully, very carefully

A possible failure mode

Ontological failure: The phenomenon you are interested in requires elements or laws outside of the set you have been given.

There is a second possible failure mode

Epistemological failure: You have enough elements and the laws do apply, but you yourself cannot understand the explanation that they provide.

D. Bray. Reductionism for biochemists: how to survive the protein jungle. *Trends Biochem.Sci.* 22 (9):325-326, 1997.

The solution to epistemological failure

Get a smarter, bigger brain…

How do we accelerate biological discovery?

What are the limits to what a community of people can learn?

VI∫BRE

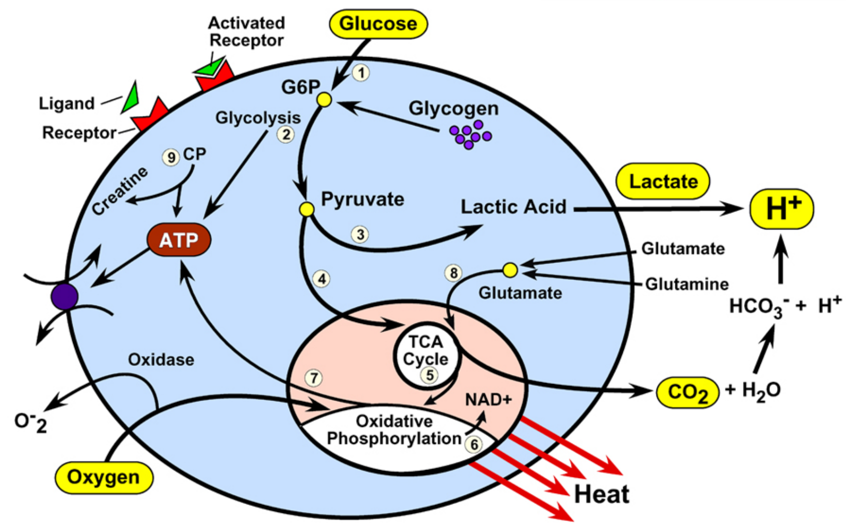
- For one person, we had

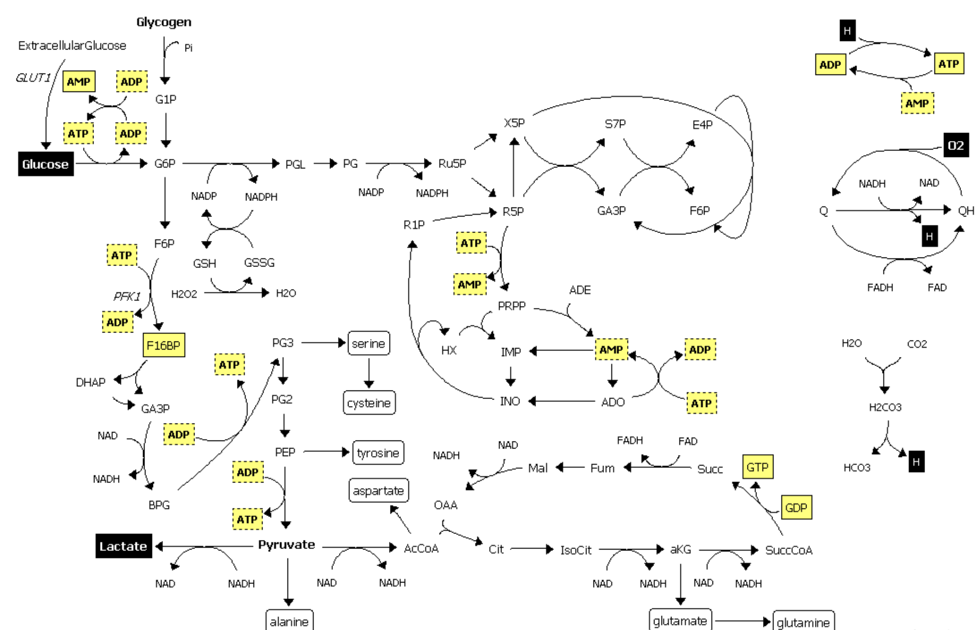
$$dK/dt = k_L Q_{IN} W_L - k_F K W_F + k_S K W_S + k_M M(W_L + W_S - W_F) + k_T K W_T$$

- Let's just add N people, each of whose brain has capacity K_{max} …
- With collective intelligence, the learning rate may scale as $dK/dt\ N^{\gamma}$, $\gamma > 1$
- Maximum brain capacity NK_{max} scales with N
- Distributed memory may reduce knowledge evaporation rate $k_F K W_F$
- Improved learning from mistakes due to redundant error checking
- With experience, utilize knowledge compression to increase $K_{max}^{effective}$
  - Simplifications
  - Connections
- There will still be problems we can't solve fast enough.
- Enter artificial intelligence, machine learning, and robot scientists!

JPW's 2006 Note to Self

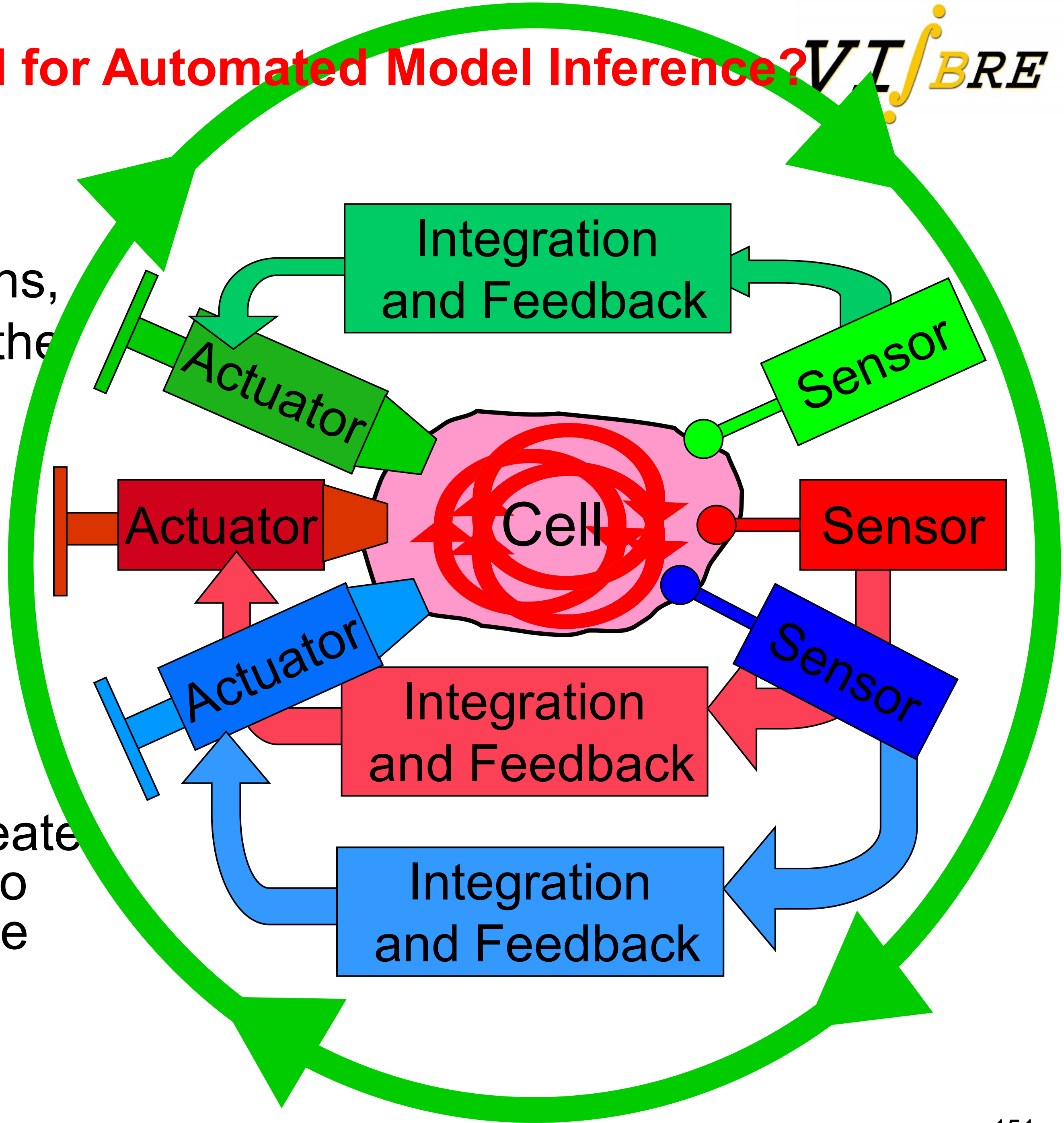
- Design and build a hybrid silicon/biological system that proposes and generates models and conducts experiments on itself to identify the underlying equations that govern the biology.
- Extracellular: $3 - 4 million and 3 - 5 years
- Intracellular: $15 - 20 million and 5 – 10 years





What Do We Need for Automated Model Inference?

- Multiple, fast **sensors**
- **Openers** (mutations, siRNA, drugs) for the internal feedback loops
- Intra- and extracellular **actuators** **for controlled perturbations**
- Algorithms that create **feedback loops** to automatically probe the system
- …



Wikswo Robot Science, 2009-2015

Grant 122. National Academies Keck Future Initiatives, "Biology on Demand: External Control of a Complex Cellular System, S. cerevisiae," 2009-2011, $50,000

Grant 124. NIH/NIDA, "Elucidation of Leukocyte and Macrophage Biomarker Signatures from Drugs of Abuse," 2009-2011, $2,661,005, (Multi-PI: John McLean, John Wikswo, Hod Lipson)

Grant 127. EMD Millipore Corporation, "The EMD Millipore Research Associate in Automated Systems Biology," 2011-2012, $85,565

Grant 128. Defense Threat Reduction Agency, "Automated Characterization of the Interaction Dynamics between Toxic Chemicals and Biological Agents and Biomolecules and Cells of Blood and Lymph," 2009-2014, $2,499,763

Inferring Metabolic Models using the SRA andEEA

Computational Synthesis

Target Model placed in black box with 10% noise

$$\frac{dS_1}{dt} = 2.5 - \frac{100 * A_3 S_1}{1 + 13.68 * A_3^4}$$

$$\frac{dS_2}{dt} = \frac{200 * A_3 S_1}{1 + 13.68 * A_3^4} - 6 * S_2 \boxed{-6 * S_2 N_2}$$

$$\frac{dS_3}{dt} = 6 * S_2 - 6 * N_2 S_2 - 64 * S_3 + 16 * A_3 S_3$$

$$\frac{dS_4}{dt} = 64 * S_3 - 16 * A_3 S_3 - 13 * S_4 - 100 * N_2 S_4 + 13 * S_5$$

$$\frac{dN_2}{dt} = 6 * S_2 - 18 * N_2 S_2 - 100 * N_2 S_4$$

$$\frac{dA_3}{dt} = -1.28 * A_3 - \frac{200 * A_3 S_1}{1 + 13.68 * A_3^4} + 128 * S_3 + 32 * A_3 S_3$$

$$\frac{dS_5}{dt} = 1.3 * S_4 - 3.1 * S_5$$

Model inferred without any a priori information

$$\frac{dS_1}{dt} = 2.53 - \frac{98.79 \cdot A_3 S_1}{1 + 12.66 \cdot A_3^4}$$ Glucose

$$\frac{dS_2}{dt} = \frac{200.23 \cdot A_3 S_1}{1 + 13.80 \cdot A_3^4} - 6.87 \cdot S_2 \boxed{-6.87 \cdot N_2 + 0.95}$$ G3P DP Pool

$$\frac{dS_3}{dt} = 6.00 \cdot S_2 - 6.00 \cdot N_2 S_2 - 64.16 \cdot S_3 + 16.08 \cdot A_3 S_3$$ BPG

$$\frac{dS_4}{dt} = 64.04 \cdot S_3 - 16.03 \cdot A_3 S_3 - 13.03 \cdot S_4 - 100.11 \cdot N_2 S_4 + 13.21 \cdot S_5$$ Pyr Act Pool

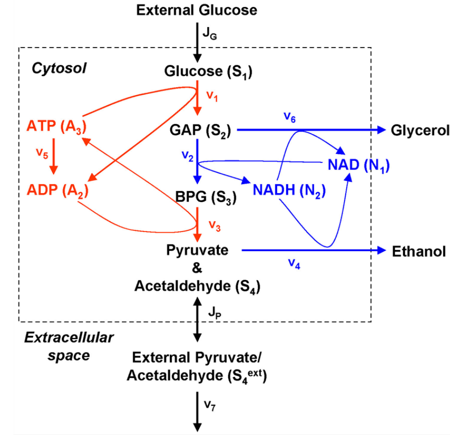
$$\frac{dN_2}{dt} = \boxed{-0.055} + 5.99 \cdot S_2 - 17.94 \cdot N_2 S_2 - 98.82 \cdot N_2 S_4$$ NADH

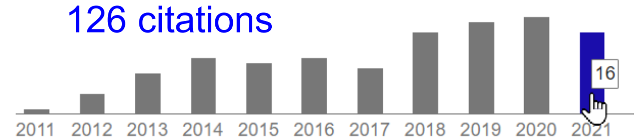
$$\frac{dA_3}{dt} = -1.12 \cdot A_3 - \frac{192.24 \cdot A_3 S_1}{1 + 12.50 \cdot A_3^4} + 124.92 \cdot S_3 + 31.69 \cdot A_3 S_3$$ ATP

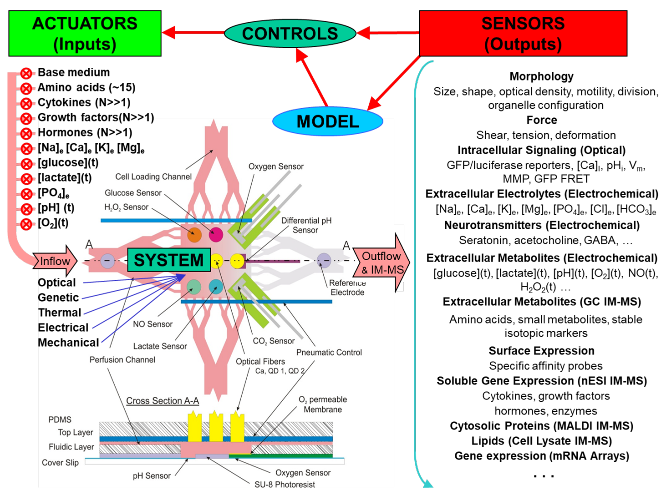
$$\frac{dS_5}{dt} = 1.23 \cdot S_4 - 2.91 \cdot S_5$$ $S4_{ext}$

Schmidt, Vallabhajosyula, Jenkins, Hood, Soni, Wikswo, and Lipson. Automated probing and inference of analytical models for metabolic networks. Phys.Biol. 8 (5):055011, 2011.

Model adapted from P. Ruoff et al. Biophysical Chemistry 106 (2003) 179-192

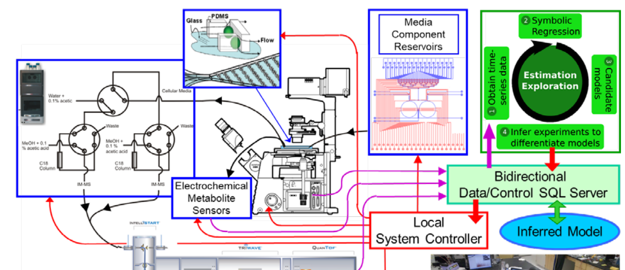






LeDuc, Messner, Wikswo, Annual Reviews of BME, 2011.

2014: VIIBRE's Robot Scientist for Automated Omni-Omics



Supported in part by DTRA and NIH/NIDA

Cornell's robot can control VIIBRE's robot microscope!

There is yet one more potential problem…

- We may not be able to understand what the computer tells us about biology.
- The next challenge is to create computers that can explain their findings to us….

- It might be as hopeless as explaining Shakespeare to a dog.

Hod Lipson, 2009

All May Not Be Lost

See Spot Read: Willow the Dog understands written commands

“….the dog can now sit up when a card says ‘Sit Up,’ plays dead when a card reads ‘Bang,’ and wave a paw when a sign says ‘Wave.’ ”

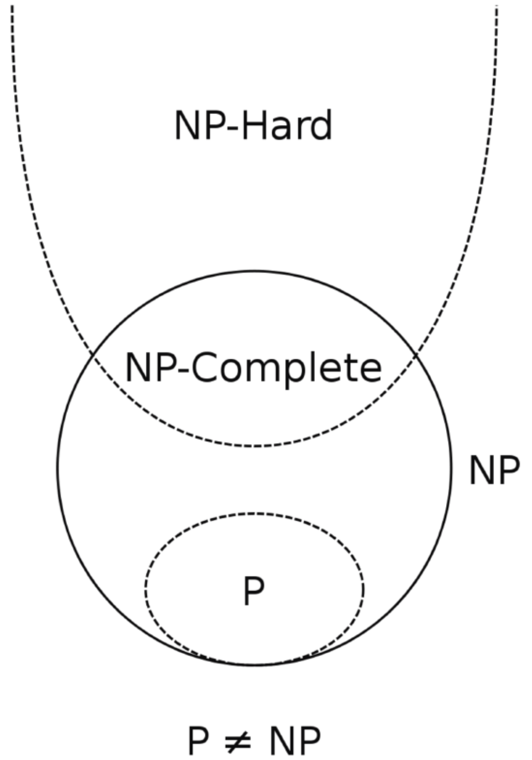
http://www.peoplepets.com/news/amazing/see-spot-read-willow-the-dog-understands-written-commands/1

The Future of Biology

How hard will it be to describe the multiscale complexity of a biological system?

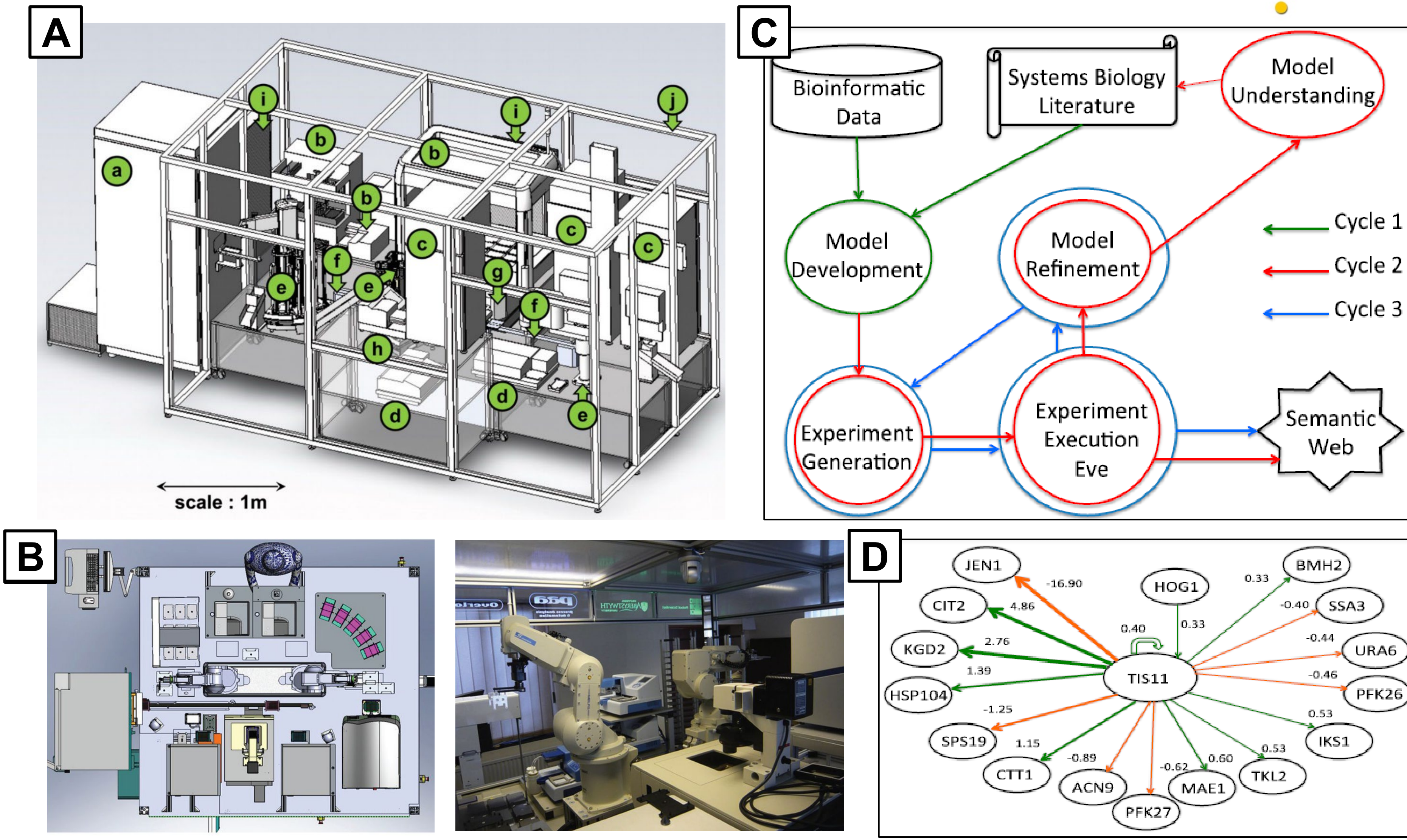
Is biology NP-complete?
NP-hard?

Finding a solution is more difficult than confirming it.



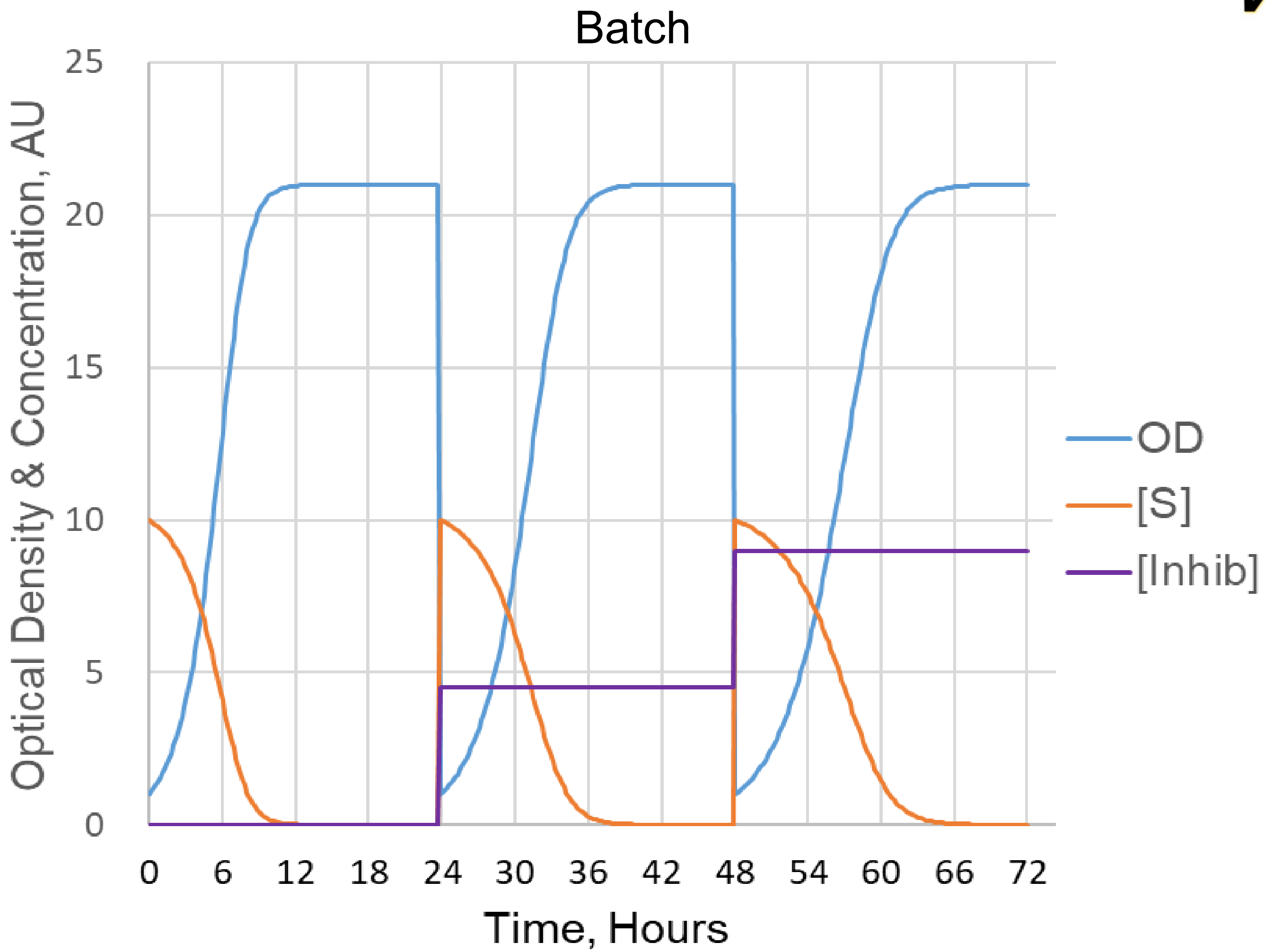
http://en.wikipedia.org/wiki/NP-hard

Ross King's Robot Scientists



A) Adam, with an automated –20°C freezer, three liquid handlers, three automated +30°C incubators, two automated plate readers, three robot arms, two automat-ed plate slides, an automated plate centrifuge, an automated plate washer, two high-efficiency particulate air filters, and a rigid transparent plastic enclosure. Autonomously, Adam specified and recorded 6,657,024 optical density measurements@595nm to form 26,495 growth curves, and formulated and tested 20 hypotheses concerning genes encoding 13 orphan enzymes.1 10 B) Eve, constructed at the University of Manchester and now being reassembled at CUT, combined multiple software tools with integrated laboratory robotics to execute C) three semiautomated cycles of diauxic shift model improvement. All the experiments were formalized and communicated to Eve's cloud laboratory automation system for execution to expand the current model of the yeast diauxic shift. The final model adds a substantial amount of knowledge: 92 genes (+45%) and 1,048 interactions (+147%), illustrated in part in D). King et al., Comp. 2009;. Williams et al., J R Soc Interface, 2015; Coutant, et al., PNAS, 2019.

Microbial culture: Batch versus continuous

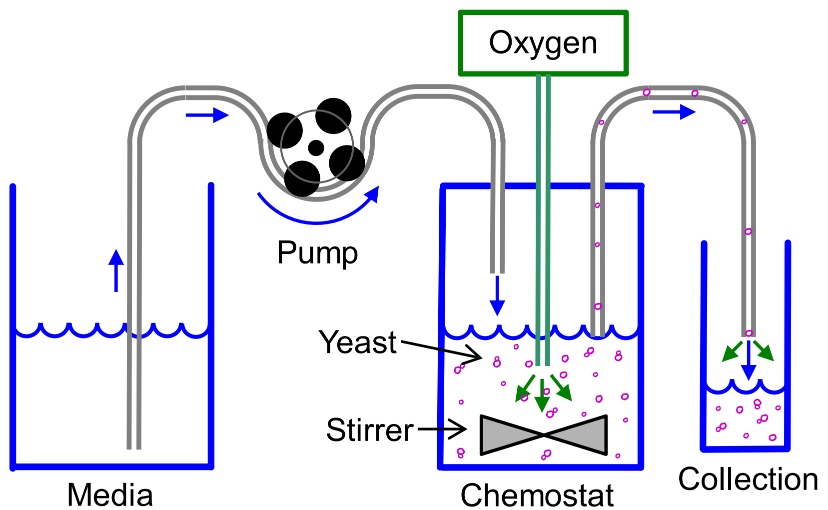


Three serial-batch measurements of yeast growth with differing inhibitor concentrations.

In batch culture, gene expression profiles change throughout the growth phase, with continuously changing levels of nutrients, metabolites, and signaling molecules. Quantifying the growth curve is hard. This may not matter for an end-point analysis.

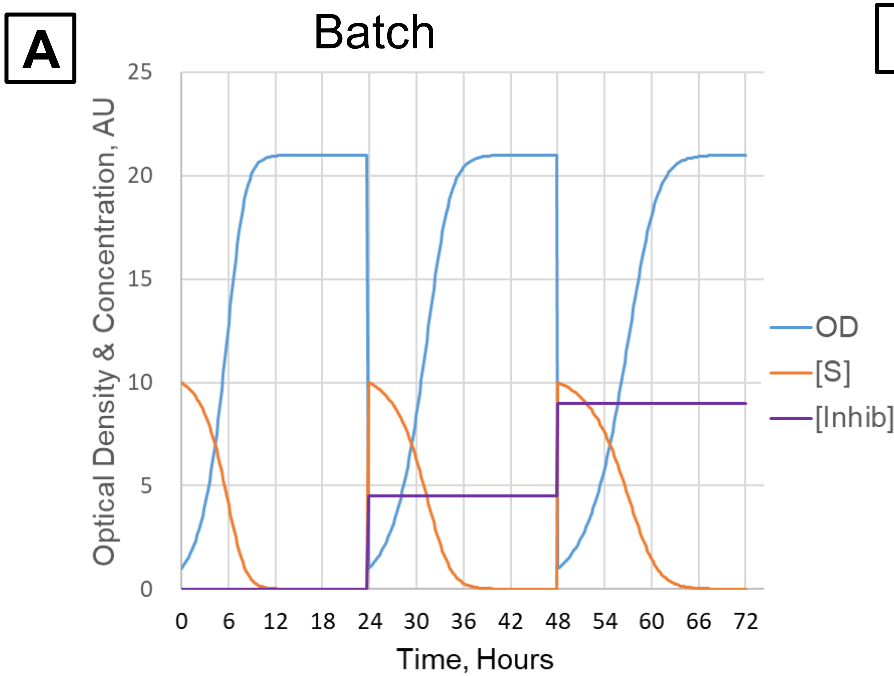
And Ross King asks me ...

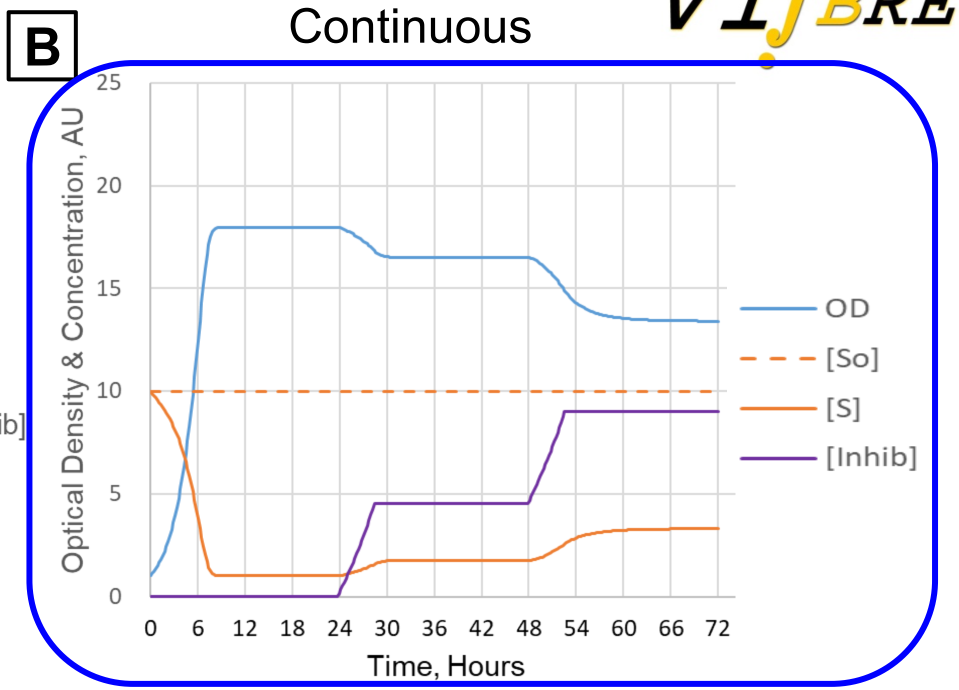
"John, can you build me a 4,000 channel chemostat for my third robot scientist, Genesis?



X 4000

Microbial culture: Batch versus continuous





A) Three serial-batch measurements of yeast growth with differing inhibitor concentrations.

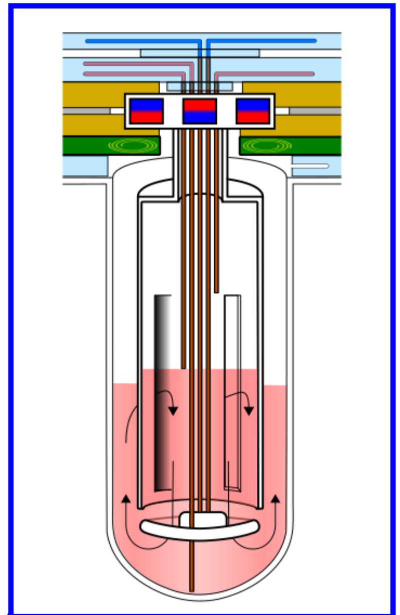
B) A continuous-perfusion chemostat experiment that after seeding reaches a steady state growth rate that represents a balance between inflow of media with the rate-limiting nutrient and efflux of cells and media. The inhibitor concentration can be changed without reseeding the bioreactor.

A) In batch culture, gene expression profiles change throughout the growth phase, with continuously changing levels of nutrients, metabolites, and signaling molecules. This may not matter for an end-point analysis.

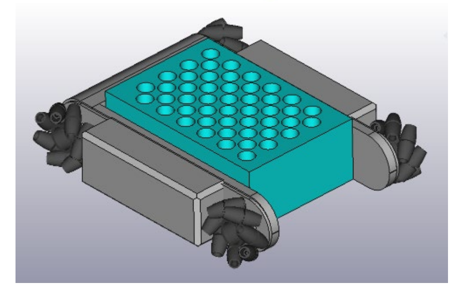
B) In chemostats, gene expression profiles are relatively constant for long periods of time, which is ideal for quantitative multi-omic measurements of signaling and metabolism required for network reconstruction.

The Genesis Project

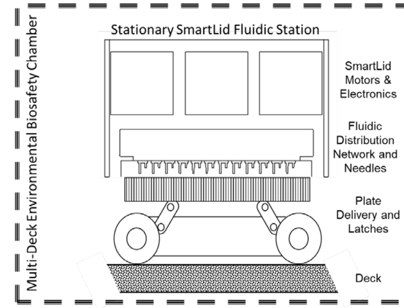
- Three stages
  - Genesis 1.0: 12 channels
  - Genesis 2.0: 48 channels
  - Genesis 3.0: 1,728 channels



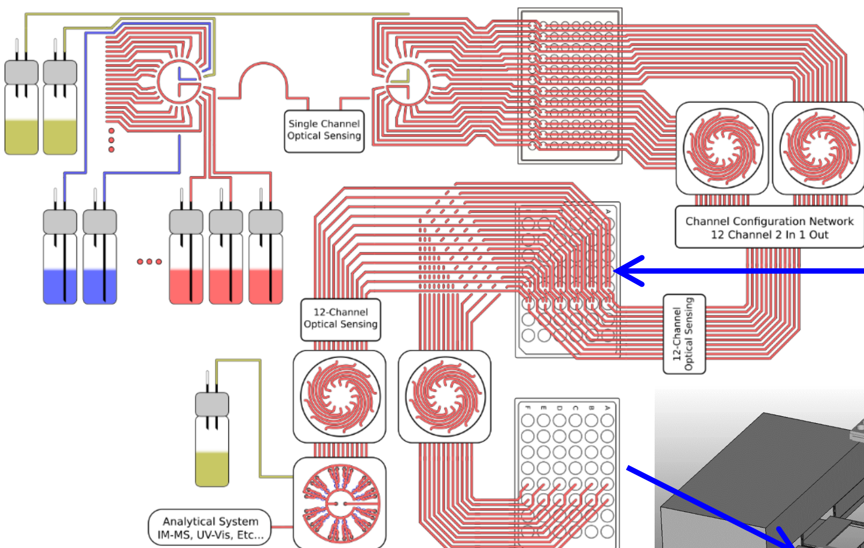
1.5 mL 48-Well Chemostat



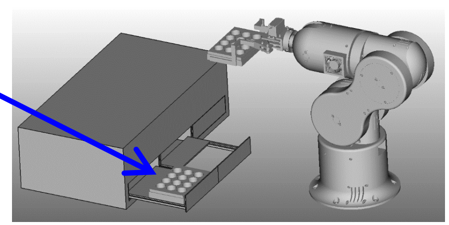
iPlateBot Transporter



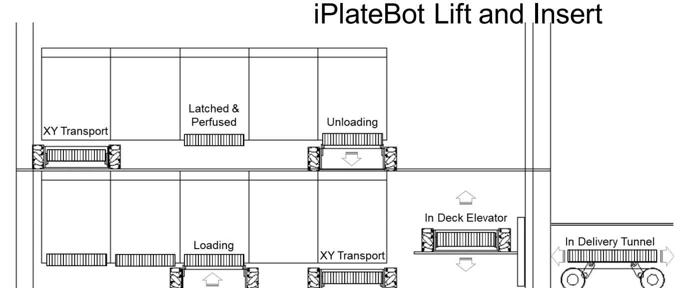
iPlateBot Lift and Insert



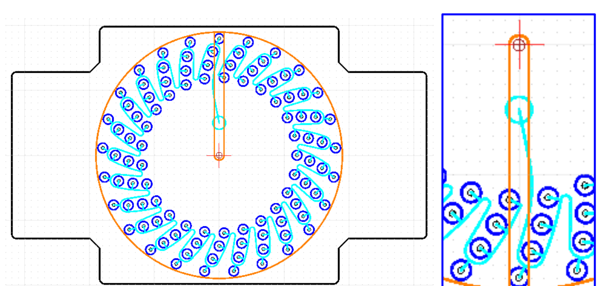
48-Well Module



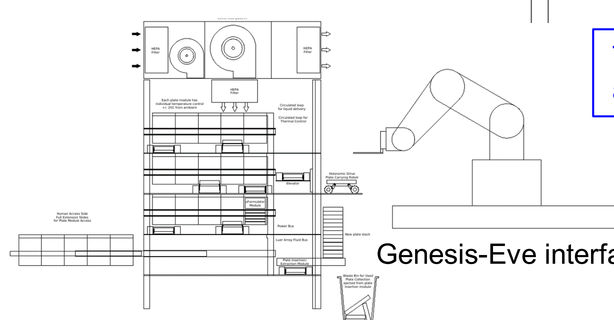
Benchtop Module Enclosure



iPlateBot 3D navigation



100-port Centi-Valve



Genesis-Eve interface

The effluent of each Genesis chemostat will be analyzed in real time by mass spectrometers.

Funding to date:

- Wallenberg Foundations to Ross King, $2,000,000
- MRI NSF-Vanderbilt grant $1,400,000
- NCATS $200,000

Driving forces for the future of Biology

- The need for more realistic *in vitro* experiments
  - Massively parallel, cellular microenvironments for the study of cell-cell, cell-cell-drug, and cell-cell-drug-snp interactions
  - Real-time control of biological systems
- The need to control multiple parameters at the same time and measure multiple dynamic variables
  - Cell-scale sensors and actuators
  - Experiments that involve thousands of parameters
- The need to create complex, nonlinear models
  - Symbolic regression and exploration-estimation algorithms for machine learning in automated microbioreactors
  - Models to enable control of cellular responses and biomolecule production
- The need to raise research funds from more diverse sources
- The inability of the human mind (or at least those of the reviewers) to understand the complexity of what is discovered
- Artificial intelligence to the rescue?

Reviewing in an interdisciplinary age

Biophysics Reviews EDITORIAL scitation.org/journal/bpr

Building Creatives in an Anti-da Vinci Age

Cite as: Biophysics Rev. **2**, 020401 (2021); doi: 10.1063/5.0059753
Submitted: 11 June 2021 · Accepted: 14 June 2021 ·
Published Online: 30 June 2021

Michael Rosnach and Kevin Kit Parker[a)]

AFFILIATIONS

150 Western Avenue, Boston, Massachusetts, 02134, USA

[a)]Author to whom correspondence should be addressed: kkparker@g.harvard.edu

When we peer review a paper, a grant application, or an academic promotion packet, the biggest challenge is assembling a jury of peers to assess the work, the proposed work, or the candidate. How the work, or promotion candidate, is branded, makes a difference in how study sections and review panels are populated. The jury's experience, fields of expertise, willingness to do the review, and availability are important determining factors. As a general rule, we are looking for the like-minded brands in the field who are best qualified to assess specialized work.

So, how do we assess transdisciplinary work? This is certainly a challenge in certain scientific circles. Consider, by way of example, the following anecdote: A couple of years ago, a panel considered nominees for an award in an interdisciplinary field. One of the candidates was presented by a panel member and a discussion ensued of how the candidate's work spanned broadly across several fields in addition to the work in the field to be awarded. At the end of the discussion, the panel director instructed the note keeper to record, as the final comment on the broadly impressive work of the nominee, that the candidate "…lacked focus."

manage the biomedical training pipelines responsible for producing highly specialized, monodisciplinary scientists with a tendency to reductionism. However, one might hypothesize that full integration of disciplines is easier to achieve in a single person because there is less latency, avoiding the communication problems between individuals of different experience, culture, or training.

Today's integrators are often found as leaders of industry or academic institutions of dedicated purpose, where their scientific and technical capabilities are less apparent than the leadership skills required of the enterprise they direct. In the case of the aforementioned award panel calling out a transdisciplinary nominee as lacking "focus," the director of the panel may have been challenged by the integrative vision, leadership skills, and experience required to guide the panel in the parallel processing effort necessary to recognize, and appreciate, the emergent creativity and innovation of the seemingly unfocused candidate. Such an effort is a messier natural process requiring a collective "learning" not afforded by the directed mandate of the society sponsoring the award.

We revere Leonardo da Vinci's transdisciplinary body of work,

Biophysics Reviews EDITORIAL scitation.org/journal/bpr

Building Creatives in an Anti-da Vinci Age

Cite as: Biophysics Rev. **2**, 020401 (2021); doi: 10.1063/5.0059753
Submitted: 11 June 2021 · Accepted: 14 June 2021 ·
Published Online: 30 June 2021

View Online Export Citation CrossMark

Michael Rosnach and Kevin Kit Parker[a)]

AFFILIATIONS

150 Western Avenue, Boston

[a)]Author to whom correspo

When we peer review a
demic promotion packet, the b
peers to assess the work, the p
the work, or promotion candid
how study sections and review p
ence, fields of expertise, willing
are important determining fact
for the like-minded brands in t
specialized work.

So, how do we assess tran
challenge in certain scientific ci
following anecdote: A couple o
nees for an award in an interd
was presented by a panel mem
candidate's work spanned broa
the work in the field to be awa
panel director instructed the n
ment on the broadly impressiv
date "...lacked focus."

It is a good bet that Leonardo da Vinci would not be granted tenure at Harvard University. It is a reasonable bet that he would not be hired in the first place, as a faculty committee would be challenged not only to assess his work, and identify comparees and letter writers, but to decide if he belongs in a department of anatomy, art, or engineering. If we can agree on this difficulty, then how should we remodel the training of "creatives" like da Vinci? Do we erroneously assume that a creative mechanical engineer would have more in common with mechanical engineers than a creative artist? Do we recognize how the tribalism of academic disciplines has artificially segmented, at the expense of the most creative, the community of scholars? Can academies take on the challenges and responsibilities of a new frontier in training da Vinci-like creatives, or will we continue to pride ourselves on minting narrowly relevant, scientific monogamists?

Lessons Learned

Lessons Learned

- The developmental trajectory of a progenitor cell can be randomly determined by a key transcription factor that has a very low copy number ($\leq \sim 10$).
- The developmental trajectory of a young interdisciplinary scientist working at a small university with a small number of possible collaborators can also be random.
- Unless you like working alone, pick very good collaborators.
- By connecting disciplines, I have helped build the foundations needed to solve a number of unrelated scientific problems.
- I am far from a Doc Brown and vastly further from a da Vinci, but I'm satisfied with the contributions I have made and am still able to make to a breadth of fields in science and engineering.
- The challenge is to figure out when to start a new project…

  You've got to know when to hold 'em
  Know when to fold 'em
  Know when to walk away
  And know when to run

  Rodgers, K, 1978

If you want to find new keys to biology, don't limit your explorations to beneath the streetlights.

John Wikswo